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=> File medline biosis embase scisearch caplus wpids
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.42       0.42

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=> e Kiessling
E1            1     KIESSLGUHR/BI
E2            1     KIESSLICH/BI
E3           54 --> KIESSLING/BI
E4            1     KIESSLSAUREAUSSCHEIDUNG/BI
E5            2     KIESSWETTER/BI
E6            3     KIEST/BI
E7           12     KIESTER/BI
E8            1     KIESTERBACH/BI
E9            3     KIESTERI/BI
E10           1     KIESTLER/BI
E11           2     KIESTRA/BI
E12           1     KIESTRUS/BI

=> s e3
L1           54 KIESSLING/BI

=> dup rem
ENTER L# LIST OR (END):l1
PROCESSING COMPLETED FOR L1
L2           44 DUP REM L1 (10 DUPLICATES REMOVED)

=> d ti hit 1-44

L2   ANSWER 1 OF 44  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Crystalline muscle phosphorylase: I. Preparation, properties, and
     molecular weight
AB   In 1936 glucose-1-phosphate was isolated from minced and washed frog
     muscle which had been incubated in phosphate buffer with traces of
     adenylic acid (1).  It was shown that the ester was formed from glycogen
     by the reaction, glycogen + inorg. phosphate → glucose-1-phosphate.
     The enzyme which catalyzed this reaction was called phosphorylase; its
     presence in mammalian tissues (muscle, heart, brain, liver) and in yeast
     was demonstrated (2); phosphorylase was shown to play an important role in
     the formation of blood sugar in the liver (3).  In 1939 the reversibility
     of the reaction was shown for yeast phosphorylase by Kiessling
     (4) and for the mammalian phosphorylases by Cori, Schmidt, and Cori (5).
     In 1940 Hanes (6) described the presence of phosphorylase in peas and
```

Inventor Search
-none of the associated compound of this record match the elected species.
Shibuya 09/815,296

L17 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:713652 HCAPLUS
DOCUMENT NUMBER: 135:271869
ENTRY DATE: Entered STN: 28 Sep 2001
TITLE: Methods and reagents for **regulation** of cellular responses in biological systems
INVENTOR(S): **Kiessling, Laura L.; Strong, Laura E.; Gestwicki, Jason E.**
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: G01N
CLASSIFICATION: 15-1 (Immunochemistry)
Section cross-reference(s): 2, 3, 9
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001071309	A2	20010927	WO 2001-US9174	20010321
WO 2001071309	A3	20030515		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001081499	A5	20011003	AU 2001-81499	20010321
US 2003125262	A1	20030703	US 2001-815296	20010321
EP 1334118	A2	20030813	EP 2001-959934	20010321
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004512258	T2	20040422	JP 2001-569247	20010321
PRIORITY APPLN. INFO.:			US 2000-191014P P	20000321

WO 2001-US9174 W 20010321

ABSTRACT:
This invention provides multivalent ligands which carry or display at least one recognition element (RE), and preferably a plurality of recognition elements, for binding directly or indirectly to cells or other biol. particles or more generally by binding to any biol. mol. The multivalent ligands provided can most generally function for binding or targeting to any biol. particle or mol. and particularly to targeting of cells or cell types or viruses, for cell aggregation and generally for macromol. assembly of biol. macromoleculares. The multivalent ligands of this invention are generally applicable for creating scaffolds (assemblies) of chemical or biol. species, including without limitation, antigens, epitopes, ligand binding groups, ligands for cell receptors (cell surface receptors, transmembrane receptors and cytoplasmic receptors), various macromols. (nucleic acids, carbohydrates, saccharides, proteins, peptides, etc.). In these scaffolds, the number, spacing, relative positioning and relative orientation of recognition elements can be controlled. Multivalent ligands of this invention can carry or display at least one signal recognition element (SRE), and preferably a plurality of signal recognition elements, and modulate biol. responses in biol. systems. The invention also relates to methods for aggregating biol. particles and macromols. and for modulating biol. response employing the multivalent ligands provided.

SUPPL. TERM: immune cell surface receptor epitope immunomodulation;
multivalent ligand virus cell signal transduction; macromol
aggregation multivalent ligand signal recognition; cancer
cell lymphocyte surface receptor signal

INDEX TERM: Cell activation
Cell proliferation

(B cell, modulation; methods and reagents for regulation

of cellular responses in biol. systems)

INDEX TERM: Proteins, specific or class

ROLE: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(SU (surface); methods and reagents for regulation of

cellular responses in biol. systems)

INDEX TERM: Cell activation

Cell proliferation

(T cell, modulation; methods and reagents for regulation

of cellular responses in biol. systems)

INDEX TERM: B cell (lymphocyte)

T cell (lymphocyte)

(activation, modulation; methods and reagents for

regulation of cellular responses in biol. systems)

INDEX TERM: Immunoassay

(agglutination test; methods and reagents for regulation

of cellular responses in biol. systems)

INDEX TERM: Antigens

ROLE: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(autoantigens; methods and reagents for regulation of

cellular responses in biol. systems)

INDEX TERM: Infection

(bacterial; methods and reagents for regulation of

cellular responses in biol. systems)

INDEX TERM: Particles

(bio-; methods and reagents for regulation of cellular

responses in biol. systems)

INDEX TERM: Macromolecular compounds

ROLE: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study,

unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(biol.; methods and reagents for regulation of cellular responses in biol. systems)
INDEX TERM: Biology
(biological action; methods and reagents for regulation of cellular responses in biol. systems)
INDEX TERM: Polymers, biological studies
ROLE: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(block; methods and reagents for regulation of cellular responses in biol. systems)
INDEX TERM: Drug delivery systems
(carriers; methods and reagents for regulation of cellular responses in biol. systems)
INDEX TERM: Chemotactic factors
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(chemoattractant; methods and reagents for regulation of cellular responses in biol. systems)
INDEX TERM: Neutrophil
(chemotaxis; methods and reagents for regulation of cellular responses in biol. systems)
INDEX TERM: Polymers, biological studies
ROLE: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-; methods and reagents for regulation of cellular responses in biol. systems)
INDEX TERM: Natural products, pharmaceutical
ROLE: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(drugs; methods and reagents for regulation of cellular responses in biol. systems)

INDEX TERM: Blood vessel
(endothelium; methods and reagents for regulation of cellular responses in biol. systems)
INDEX TERM: Immunoassay
(enzyme-linked immunosorbent assay; methods and reagents for regulation of cellular responses in biol. systems)
INDEX TERM: Biofilm bacteria
(formation; methods and reagents for regulation of cellular responses in biol. systems)
INDEX TERM: Neoplasm
(growth inhibition; methods and reagents for regulation of cellular responses in biol. systems)
INDEX TERM: Immunoassay
(immunoblotting; methods and reagents for regulation of cellular responses in biol. systems)
INDEX TERM: Immunoassay
(immunohistochem. staining; methods and reagents for regulation of cellular responses in biol. systems)
INDEX TERM: Enzymes, biological studies
ROLE: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(label; methods and reagents for regulation of cellular responses in biol. systems)
INDEX TERM: Neoplasm
(metastasis, inhibition; methods and reagents for regulation of cellular responses in biol. systems)
INDEX TERM: Polymerization
(metathetic, ring-opening, scaffold; methods and reagents for regulation of cellular responses in biol. systems)
INDEX TERM: Animal
Animal cell
Apoptosis
B cell (lymphocyte)
Biochemical molecules
Cell aggregation
Cell junction

Chemotaxis
Coupling agents
Drug delivery systems
Drugs
Epithelium
Epitopes
Eukaryote (Eukaryotae)
Fluorescent substances
Gram-negative bacteria
Gram-positive bacteria (Firmicutes)
Immune tolerance
Immunity
Labels
Leukocyte
Lymphocyte
Mammal (Mammalia)
Microorganism
Neutrophil
PCR (polymerase chain reaction)
Parasite
Pathogen
Prokaryote
Signal transduction, biological
T cell (lymphocyte)
Virion structure
Virus
(methods and reagents for regulation of cellular responses in biol. systems)

INDEX TERM: Amino acids, biological studies
Antigens
Carbohydrates, biological studies
Cytokines
Disaccharides
Glycoproteins, general, biological studies
Growth factors, animal
Haptens
Hormones, animal, biological studies
Monosaccharides
Nucleic acids
Peptides, biological studies
Proteins, general, biological studies
Receptors
ROLE: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(methods and reagents for regulation of cellular responses in biol. systems)

INDEX TERM: Agglutinins and Lectins
Polysaccharides, biological studies
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(methods and reagents for regulation of cellular responses in biol. systems)

INDEX TERM: CD22 (antigen)
ROLE: BPR (Biological process); BSU (Biological study,
unclassified); BIOL (Biological study); PROC (Process)
(methods and reagents for regulation of cellular responses in biol. systems)

INDEX TERM: G protein-coupled receptors
ROLE: BPR (Biological process); BSU (Biological study,
unclassified); THU (Therapeutic use); BIOL (Biological
study); PROC (Process); USES (Uses)
(methods and reagents for regulation of cellular responses in biol. systems)

INDEX TERM: Antibodies
Biopolymers
Polyesters, biological studies
Polyethers, biological studies
Polymers, biological studies
Radionuclides, biological studies
ROLE: BSU (Biological study, unclassified); THU (Therapeutic
use); BIOL (Biological study); USES (Uses)
(methods and reagents for regulation of cellular responses in biol. systems)

INDEX TERM: Cell adhesion
Cell death
Cell differentiation
Cell migration
Cell proliferation
(modulation; methods and reagents for regulation of
cellular responses in biol. systems)

INDEX TERM: Ligands
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(multivalent; methods and reagents for regulation of

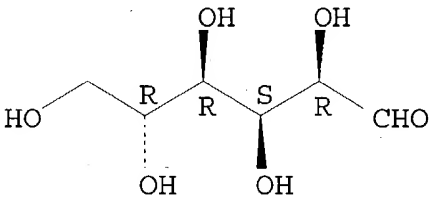
cellular responses in biol. systems)
INDEX TERM: Chemotaxis
(neutrophil; methods and reagents for regulation of
cellular responses in biol. systems)
INDEX TERM: Biological transport
(nutrient uptake; methods and reagents for regulation of
cellular responses in biol. systems)
INDEX TERM: Phosphates, biological studies
ROLE: BAC (Biological activity or effector, except adverse);
BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological
study); PROC (Process); USES (Uses)
(phosphorothioates; methods and reagents for regulation
of cellular responses in biol. systems)
INDEX TERM: Polyamides, biological studies
ROLE: BSU (Biological study, unclassified); THU (Therapeutic
use); BIOL (Biological study); USES (Uses)
(poly(amino acids); methods and reagents for regulation
of cellular responses in biol. systems)
INDEX TERM: Alcohols, biological studies
ROLE: BSU (Biological study, unclassified); THU (Therapeutic
use); BIOL (Biological study); USES (Uses)
(polyhydric; methods and reagents for regulation of
cellular responses in biol. systems)
INDEX TERM: Cell
(processes; methods and reagents for regulation of
cellular responses in biol. systems)
INDEX TERM: B cell (lymphocyte)
T cell (lymphocyte)
(proliferation, modulation; methods and reagents for
regulation of cellular responses in biol. systems)
INDEX TERM: Functional groups
(reporter; methods and reagents for regulation of
cellular responses in biol. systems)
INDEX TERM: Mutation
(substitution; methods and reagents for regulation of

cellular responses in biol. systems)
INDEX TERM: Proteins, specific or class
ROLE: BAC (Biological activity or effector, except adverse);
BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological
study); PROC (Process); USES (Uses)
(transmembrane, receptor; methods and reagents for
regulation of cellular responses in biol. systems)
INDEX TERM: Blood-group substances
ROLE: BSU (Biological study, unclassified); THU (Therapeutic
use); BIOL (Biological study); USES (Uses)
(typing; methods and reagents for regulation of cellular
responses in biol. systems)
INDEX TERM: Nutrients
(uptake; methods and reagents for regulation of cellular
responses in biol. systems)
INDEX TERM: 50-99-7, Glucose, biological studies 59-23-4, Galactose,
biological studies 11028-71-0, Con A
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(methods and reagents for regulation of cellular responses in biol. systems)
INDEX TERM: 9003-05-8 25087-26-7D, polymethacrylic acid, derivs.
59880-97-6 64364-50-7 186961-29-5D, reaction products
with galactose-containing ROMP scaffold backbones
316375-27-6
316375-27-6D, polymers, reaction products with Grubb's
ruthenium catalyst 316375-29-8 316375-29-8D, polymers,
reaction products with Grubb's ruthenium catalyst
362663-18-1 362663-18-1D, polymers, reaction products with
Grubb's ruthenium catalyst 362663-19-2
362663-20-5
ROLE: BSU (Biological study, unclassified); THU (Therapeutic

use); BIOL (Biological study); USES (Uses)
(methods and reagents for regulation of cellular responses in biol. systems)

MF C6 H12 O6
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DIOGENES, DIPPR*, GMELIN*,
IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, NAPRALERT, NIOSHTIC, PDLCOM*,
PHAR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.

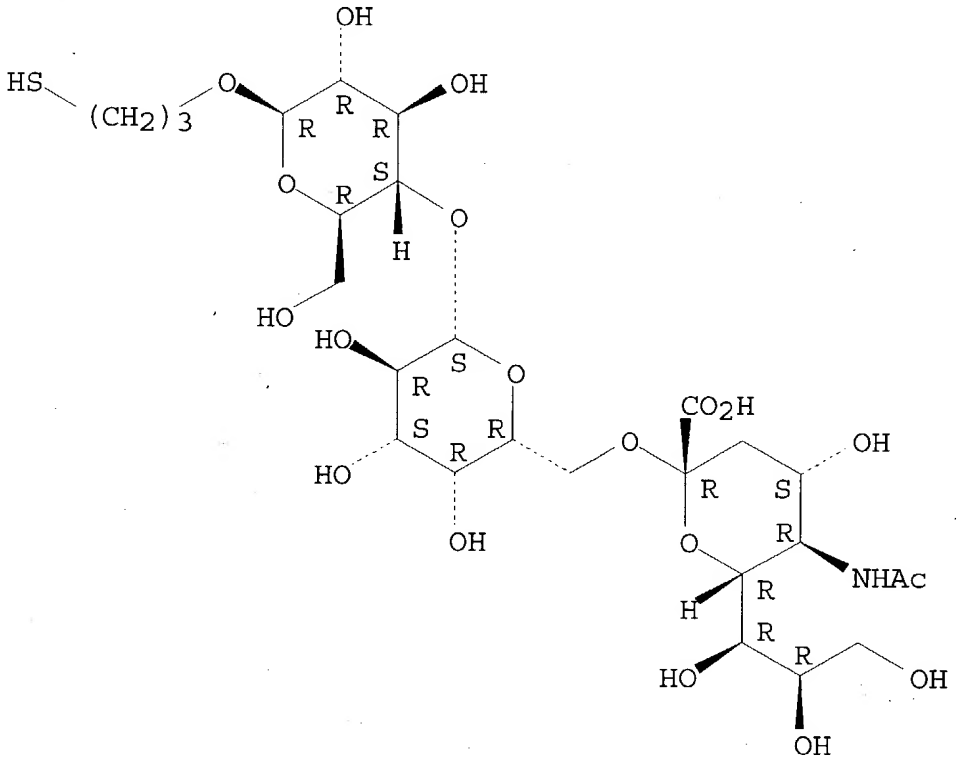


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

166721 REFERENCES IN FILE CA (1907 TO DATE)
2196 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
166981 REFERENCES IN FILE CAPLUS (1907 TO DATE)
14 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L18 ANSWER 1 OF 13 REGISTRY COPYRIGHT 2004 ACS on STN
RN **362663-20-5** REGISTRY
CN β-D-Glucopyranoside, 3-mercaptopropyl O-(N-acetyl-α-neuraminosyl)-(2→6)-O-β-D-galactopyranosyl-(1→4)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H45 N O19 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



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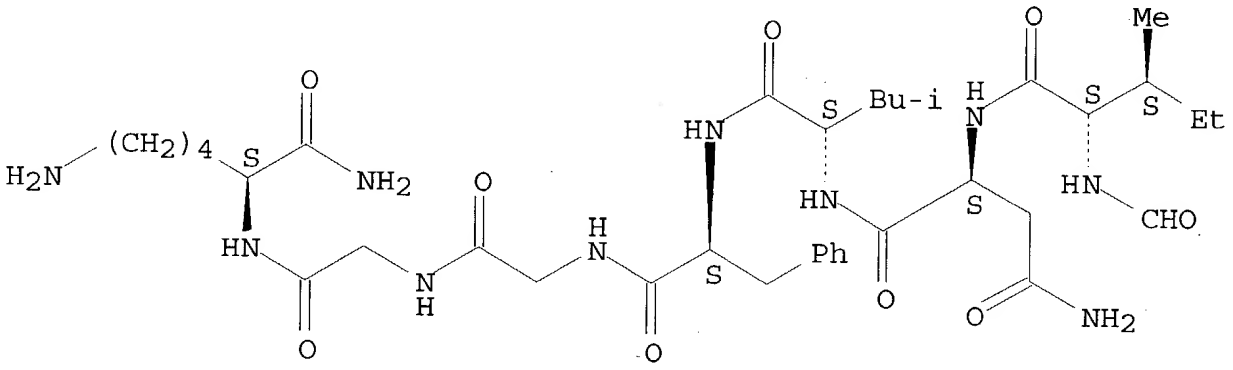
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 2 OF 13 REGISTRY COPYRIGHT 2004 ACS on STN
RN **362663-19-2** REGISTRY
CN L-Lysinamide, N-formyl-L-isoleucyl-L-asparaginyl-L-leucyl-L-

phenylalanylglycylglycyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C36 H58 N10 O9
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



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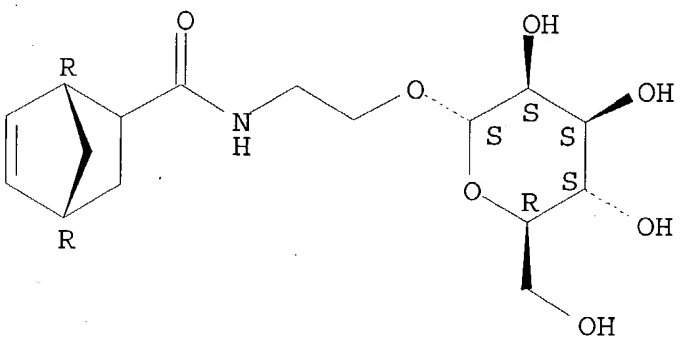
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 3 OF 13 REGISTRY COPYRIGHT 2004 ACS on STN
RN **362663-18-1** REGISTRY
CN Bicyclo[2.2.1]hept-5-ene-2-carboxamide, N-[2-(α-D-mannopyranosyloxy)ethyl]-, (1R,4R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C16 H25 N O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



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2 REFERENCES IN FILE CA (1907 TO DATE)
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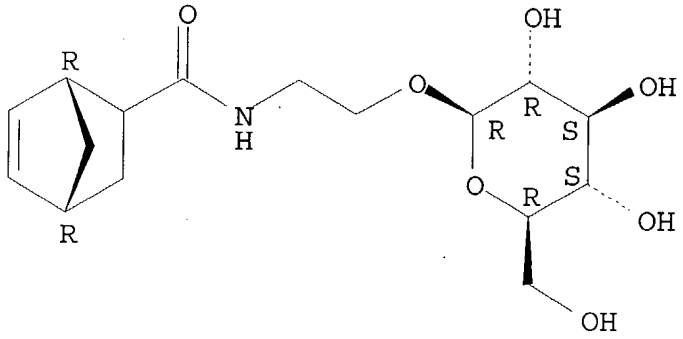
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 4 OF 13 REGISTRY COPYRIGHT 2004 ACS on STN
RN **316375-29-8** REGISTRY
CN Bicyclo[2.2.1]hept-5-ene-2-carboxamide, N-[2-(β-D-glucopyranosyloxy)ethyl]-, (1R,4R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C16 H25 N O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



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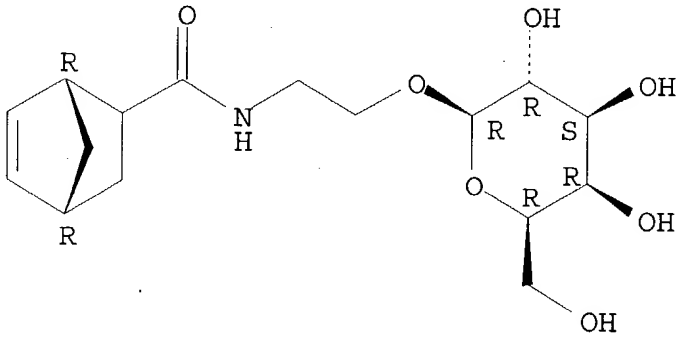
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 5 OF 13 REGISTRY COPYRIGHT 2004 ACS on STN
RN **316375-27-6** REGISTRY
CN Bicyclo[2.2.1]hept-5-ene-2-carboxamide, N-[2-(β-D-galactopyranosyloxy)ethyl]-, (1R,4R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C16 H25 N O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



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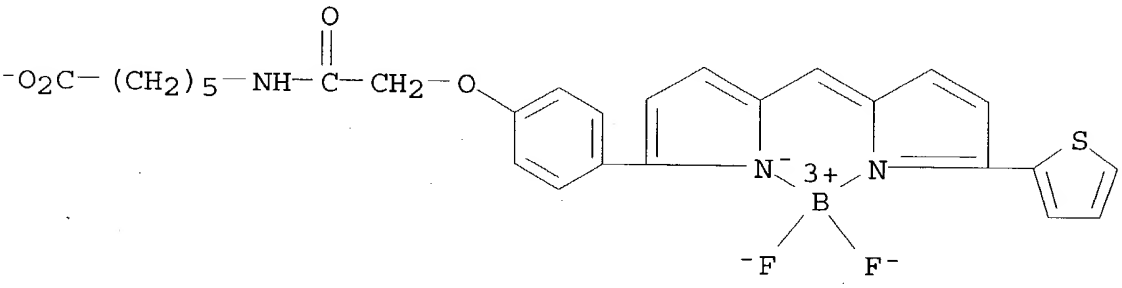
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 6 OF 13 REGISTRY COPYRIGHT 2004 ACS on STN
RN **186961-29-5** REGISTRY
CN Borate(1-),
difluoro[6-[[[4-[5-[[5-(2-thienyl)-2H-pyrrol-2-ylidene-
κN]methyl]-1H-pyrrol-2-yl-κN]phenoxy]acetyl]amino]hexanoato(2-
)]-, hydrogen, (T-4)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN BODIPY 589/616
MF C27 H25 B F2 N3 O4 S . H
CI CCS
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



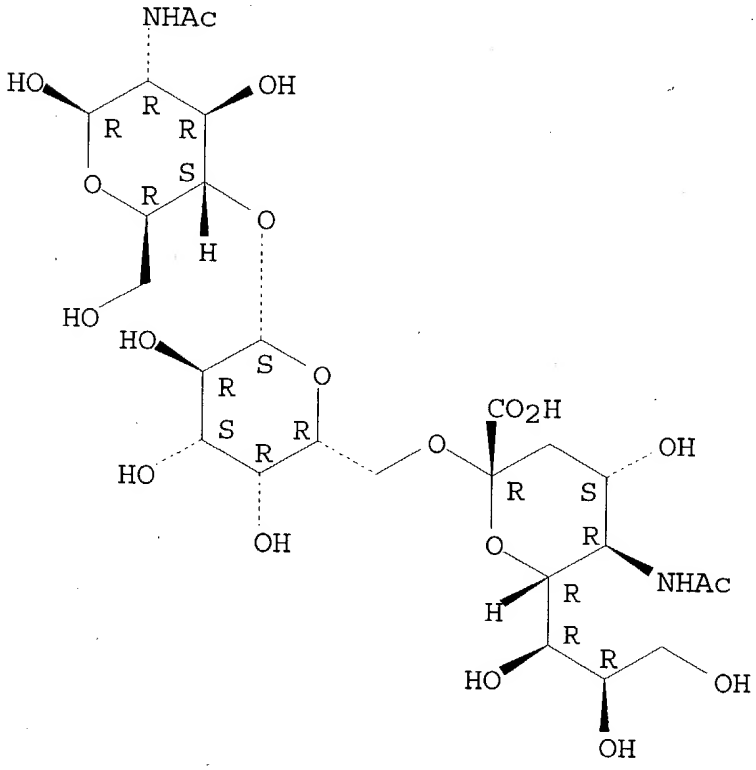
● H^+

6 REFERENCES IN FILE CA (1907 TO DATE)

3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
6 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 7 OF 13 REGISTRY COPYRIGHT 2004 ACS on STN
RN **64364-50-7** REGISTRY
CN β-D-Glucopyranose, O-(N-acetyl-α-neuraminosyl)-(2→6)-O-β-D-galactopyranosyl-(1→4)-2-(acetylamino)-2-deoxy- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C25 H42 N2 O19
CI COM
LC STN Files: BEILSTEIN*, CA, CANCERLIT, CAPLUS, CASREACT, CHEMINFORMRX, MEDLINE, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



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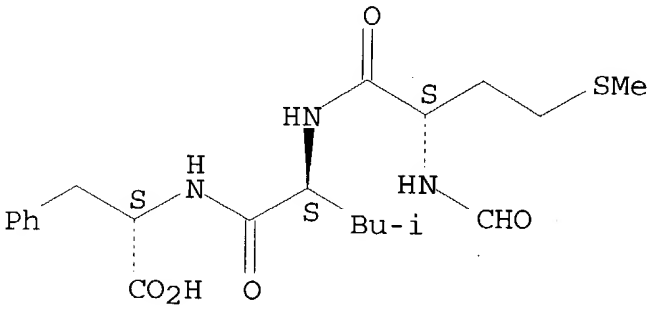
5 REFERENCES IN FILE CA (1907 TO DATE)

5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 8 OF 13 REGISTRY COPYRIGHT 2004 ACS on STN
RN **59880-97-6** REGISTRY
CN L-Phenylalanine, N-formyl-L-methionyl-L-leucyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Phenylalanine, N-[N-(N-formyl-L-methionyl)-L-leucyl]-
OTHER NAMES:
CN N-Formyl-L-methionyl-L-leucyl-L-phenylalanine
CN N-Formyl-Met-Leu-Phe-OH
CN NSC 350593
FS STEREOSEARCH
DR 75501-03-0
MF C21 H31 N3 O5 S
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CANCERLIT,
CAPLUS, CASREACT, CHEMCATS, CSCHEM, MEDLINE, MSDS-OHS, NIOSHTIC, PROMT,
TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

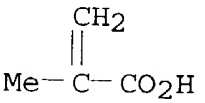
3246 REFERENCES IN FILE CA (1907 TO DATE)
56 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3247 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 9 OF 13 REGISTRY COPYRIGHT 2004 ACS on STN
RN **25087-26-7** REGISTRY
CN 2-Propenoic acid, 2-methyl-, homopolymer (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Methacrylic acid, polymers (8CI)
OTHER NAMES:

CN 90TV
CN AC 30H
CN Accelar 20
CN Acryloid AT 101
CN Acrysol 60
CN Darex 41
CN Daxad 34
CN Jurymer AC 30H
CN Methacrylic acid homopolymer
CN Methacrylic acid polymer
CN PMA
CN PMAA
CN Poly(methacrylic acid)
CN SLPI 400
CN Taicrin P
CN Versicol K 13
CN Versicol K-II
DR 115708-68-4
MF (C4 H6 O2)x
CI PMS, COM
PCT Polyacrylic
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,
CA, CANCERLIT, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM,
DDFU, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2,
IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MSDS-OHS, NIOSHTIC, PIRA, PROMT,
TOXCENTER, TULSA, USPAT2, USPATFULL, VETU, VTB
Other Sources: DSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

CM 1

CRN 79-41-4
CMF C4 H6 O2



5491 REFERENCES IN FILE CA (1907 TO DATE)
813 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5502 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 10 OF 13 REGISTRY COPYRIGHT 2004 ACS on STN
RN **11028-71-0** REGISTRY

CN Concanavalin A (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN Con A
CN Concanavaline A
CN Lectins, concanavalins A
DR 12612-33-8
MF Unspecified
CI COM, MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,
CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMLIST,
CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE,
MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PIRA, PROMT, RTECS*, TOXCENTER,
USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
8832 REFERENCES IN FILE CA (1907 TO DATE)
614 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
8837 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

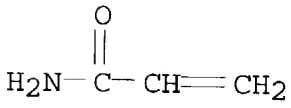
L18 ANSWER 11 OF 13 REGISTRY COPYRIGHT 2004 ACS on STN
RN **9003-05-8** REGISTRY
CN 2-Propenamide, homopolymer (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Acrylamide, polymers (8CI)
OTHER NAMES:
CN 2-Propenamide hydrochloride homopolymer
CN 2300S
CN 2J
CN 3330s
CN 38F
CN 920MPM
CN Accotrol S 622
CN Acrylamide homopolymer
CN Acrylamide polymer
CN Alcoflood 1175
CN American Cyanamid KPAM
CN American Cyanamid P 250
CN AMF
CN Aminogen PA
CN AP 273
CN Aron F 40
CN ASP 6

CN BanDrift
CN Boze Floc N 46BT
CN Calgon 470
CN Calgon 800
CN CM 303
CN CM 311
CN Cogum 20P
CN Cogum 25H
CN Colsize WLV
CN Cyanamer A 15L
CN Cyanamer N 10
CN Cyanamer N 100
CN Cyanamer N 100L
CN Cyanamer N 300
CN Cyanamer N 300LMW
CN Cyanamer P 250
CN Cyanamer P 35
CN Cytame 5
CN Diaclear MA 3000H
CN Diaclear MN 3000
CN Diaclear MN 3000H
CN Discol 4600
CN DK Dry Capsule ESP
CN DKS-ORP-F 40NT
CN Dow 164
CN Dow ET 597
CN Dow J 100
CN DP 1916
CN DP 9-6193
CN DS 415
CN E 936
CN ET 597
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for
DISPLAY
DR 12624-24-7, 9082-06-8, 122177-63-3, 57679-11-5, 129774-19-2, 133522-77-7,
25038-45-3, 104981-89-7, 114265-35-9, 51312-40-4, 68247-81-4, 72270-86-1,
79079-15-5, 143180-09-0, 143180-13-6, 143180-22-7, 143749-07-9,
27754-57-0, 33338-03-3, 39355-07-2, 39387-77-4, 200138-95-0, 443682-77-7
MF (C3 H5 N O)x
CI PMS, COM
PCT Polyacrylic, Polyamide, Polyamide formed
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA,
CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM,
CSNB, DDFU, DETHERM*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT,

ENCOMPPAT2, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MSDS-OHS,
NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, TOXCENTER, TULSA, USPAT2,
USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

CM 1

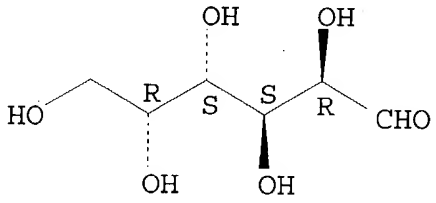
CRN 79-06-1
CMF C3 H5 N O



21518 REFERENCES IN FILE CA (1907 TO DATE)
3577 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
21552 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 12 OF 13 REGISTRY COPYRIGHT 2004 ACS on STN
RN **59-23-4** REGISTRY
CN D-Galactose (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Galactose, D- (8CI)
OTHER NAMES:
CN (+)-Galactose
CN D-(+)-Galactose
CN Galactosė
FS STEREOSEARCH
DR 147-76-2, 3812-56-4, 400876-94-0
MF C6 H12 O6
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS,
BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB,
CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE,
HODOC*, IMSRESEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR,
PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

21507 REFERENCES IN FILE CA (1907 TO DATE)
759 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
21535 REFERENCES IN FILE CAPLUS (1907 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L18 ANSWER 13 OF 13 REGISTRY COPYRIGHT 2004 ACS on STN
RN **50-99-7** REGISTRY
CN D-Glucose (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN (+)-Glucose
CN Anhydrous dextrose
CN Cartose
CN Cerelose
CN Cerelose 2001
CN Clearsweet 95
CN Clintose L
CN Corn sugar
CN CPC hydrate
CN D(+)-Glucose
CN Dextropur
CN Dextrose
CN Dextrosol
CN Glucodin
CN Glucolin
CN Glucose
CN Glucosteril
CN Goldsugar
CN Grape sugar
CN Maxim Energy Gel
CN Roferose ST
CN Staleydex 111
CN Staleydex 130
CN Staleydex 333
CN Sugar, grape
CN Tabfine 097(HS)
CN Vadex
FS STEREOSEARCH
DR 8012-24-6, 8030-23-7, 162222-91-5, 165659-51-8, 50933-92-1, 80206-31-1

Shibuya
~~Sibuya~~ 09/815,296

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L3                  STR
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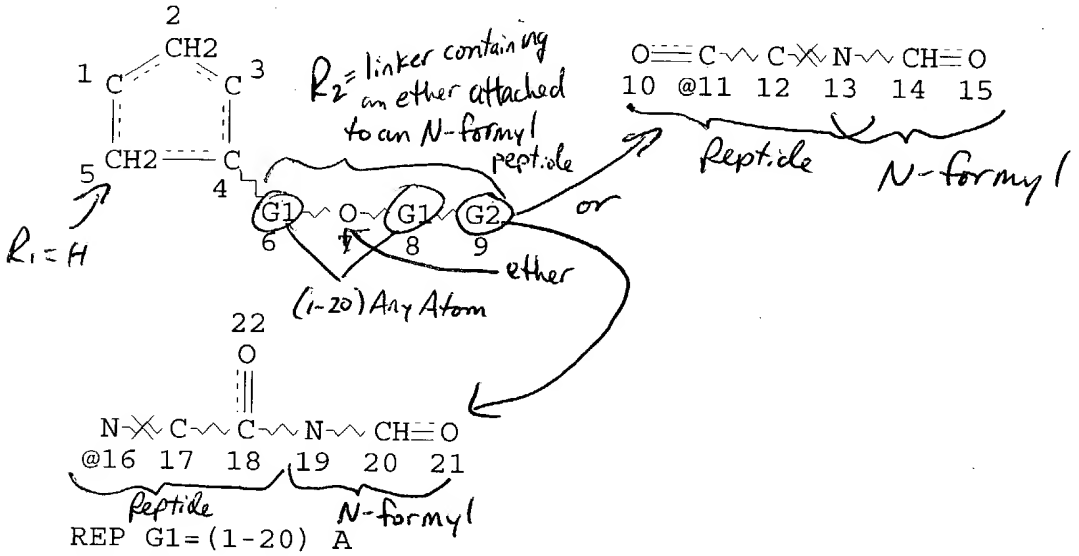


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VAR G2=11/16
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC   1
NUMBER OF NODES IS  22

STEREO ATTRIBUTES: NONE
L4          61105 SEA FILE=REGISTRY ABB=ON  PLU=ON  C5/ES AND N>1 AND
O>2
L6              0 SEA FILE=REGISTRY SUB=L4 SSS FUL L3
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Zero hits for structure search

Database Screening:

Cmpd must have:

- C5 Ring
- greater than 1 Nitrogen Atom
- greater than 2 Oxygen Atoms

*This search would have found both of the compounds on pg. 28 if they were present in the Registry file.

Shibuya
~~Sibuya~~ 09/815,296

Text Search

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?FORMYLAT?(5A)?PEPTID?
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OPENING
                METATHES? OR RE OR RECOGNITION ELEMENT OR SRE OR FE
OR
                FUNCTIONAL ELEMENT)
L9             4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND L8
L10           14 SEA FILE=REGISTRY ABB=ON  PLU=ON  (161834-86-2/BI OR
7439-89-6/
                BI OR 162382-31-2/BI OR 60-00-4/BI OR 66-71-7/BI OR
7439-96-5/B
                I OR 7782-44-7/BI OR 9001-05-2/BI OR 9001-50-7/BI OR
9001-59-6/
                BI OR 9001-60-9/BI OR 9001-83-6/BI OR 9023-70-5/BI OR
9054-89-1
                /BI)
L11            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND L10
L12            4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 OR L11


=> d l12 ibib abs hitind hitstr 1-4

L12  ANSWER 1 OF 4  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:        2001:639378  HCAPLUS
TITLE:                   Peptide Deformylase: A Target for
Antimicrobial Drug
                         Design
AUTHOR(S):               Pei, Dehua
CORPORATE SOURCE:        Department of Chemistry, The Ohio State
University,
                         Columbus, OH, 43210, USA
SOURCE:                  Abstracts of Papers, 222nd ACS National
Meeting,
                         Chicago, IL, United States, August 26-30,
2001 (2001),
                         INOR-191.  American Chemical Society:
Washington, D.
                         C.
                         CODEN: 69BUZP
DOCUMENT TYPE:           Conference; Meeting Abstract
LANGUAGE:                English
AB   Protein synthesis in prokaryotes initiates with an
N-formylmethionine-
     tRNAi, resulting in N-terminal formylation of all nascent
     polypeptides. Peptide deformylase (PDF) catalyzes the subsequent
     removal of the formyl group from the majority of bacterial
proteins.  As
```

an activity essential for bacterial survival, PDF provides an attractive target for antibacterial drug design. Recent biochem. and spectroscopic studies have revealed that PDF is a new type of **Fe**(II) metalloenzyme, which utilizes a ferrous ion to activate a water mol. for nucleophilic attack on the formyl substrate. Two approaches are being pursued to design antibacterial agents that target PDF. In the first approach, prodrugs are synthesized which have no biol. activity by themselves but can be selectively converted into cytotoxic agents by PDF in bacterial cells. In the second approach, specific PDF inhibitors have been rationally designed and synthesized based on metal chelation with 2-alkyl-3-mercaptopropionyl group as the core. The most potent inhibitor has a Ki value of 11 nM toward purified Bacillus subtilis PDF. These inhibitors act as potent antibacterial agents against all 4 bacterial strains that have been tested, with minimal inhibitory concns. (MICs) as low as 2 μg/mL. These results demonstrate that PDF is a viable target for designing novel, broad-spectrum antibacterial agents.

L12 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:332814 HCAPLUS
TITLE: Peptide deformylase: New target for antibacterial drug design.
AUTHOR(S): Pei, Dehua
CORPORATE SOURCE: Department of Chemistry, Ohio State University, Columbus, OH, 43210, USA
SOURCE: Book of Abstracts, 219th ACS National Meeting, San Francisco, CA, March 26-30, 2000 (2000), ORGN-687. American Chemical Society: Washington, D. C.
CODEN: 69CLAC
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Protein synthesis in prokaryotes initiates with an N-formylmethionyl-

tRNAi, resulting in N-terminal **formylation** of all nascent **polypeptides**. Peptide deformylase (PDF) catalyzes the subsequent removal of the formyl group from the majority of bacterial proteins. As an activity essential for bacterial survival but absent from animal cells, PDF provides an attractive target for antibacterial drug design. Recent biochem. and spectroscopic studies have revealed that the deformylase is a new type of **Fe**(II) metalloenzyme, which utilizes the ferrous ion to activate a water mol. for nucleophilic attack on the formyl substrate. Two approaches are being pursued to design antibacterial drugs that target PDF. In the first approach, prodrugs are synthesized which have no biol. activity by themselves but can be selectively converted into cytotoxic agents by PDF in bacterial cells. In the second approach, specific PDF inhibitors have been rationally designed and synthesized based on metal chelation with a 2-alkyl-3-mercaptopropionyl group as the core. The most potent inhibitor has a Ki value of 3.2 nM toward the purified Bacillus subtilis PDF. These inhibitors act as potent antibacterial agents with minimal inhibitory concns. (MICs) as low as 2 μg/mL. These results demonstrate that PDF is a viable target for designing novel, broad-spectrum antibiotics.

L12 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:313671 HCAPLUS
DOCUMENT NUMBER: 122:234924
TITLE: Isolation, purification and structure of exochelin MS, the extracellular siderophore from Mycobacterium smegmatis
AUTHOR(S): Sharman, Gary J.; Williams, Dudley, H.; Ewing, David F.; Ratledge, Colin
CORPORATE SOURCE: Cambridge Centre for Molecular Recognition, Cambridge University, Cambridge, CB2 1EW, UK
SOURCE: Biochemical Journal (1995), 305(1), 187-96
CODEN: BIJOAK; ISSN: 0264-6021

PUBLISHER: Portland Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The extracellular siderophore from M. smegmatis, exochelin MS, was isolated from **Fe**-deficiently grown cultures and purified to >98% by a combination of ion-exchange chromatog. and HPLC. The material was unextractable into organic solvents, was basic (pI = 9.3-9.5), had a λmax at 420 nm, and a probable Ks for Fe3+ of 1025-1030. Its structure was determined by examination of deferri- and ferri-exochelin and its Ga complex. The methods used were electrospray mass spectrometry and 1- and 2-dimensional (NOESY, DQF-COSY, and TOCSY) 1H NMR. The constituent amino acids were examined by chiral GLC anal. of N-trifluoroacetyl iso-Pr and N-pentafluoropropionyl Me esters after hydrolysis, and reductive HI hydrolysis, of the siderophore. The exochelin was a **formylated pentapeptide**: N-(δN-formyl,δN-hydroxy-R-ornithinyl)-β-alaninyl-δN-hydroxy-R-ornithinyl-R-allo-threoninyl-δN-hydroxy-S-ornithine. The linkages involving the 3 Orn residues were via their δN(OH) and α-CO groups leaving 3 free α-NH2 groups. Although there were 2 peptide bonds, these involved the 3 R(D)-amino acids. Thus, the mol. has no conventional peptide bond, suggesting that it will be resistant to peptidase hydrolysis. The coordination center with Fe3+ was hexadentate in an octahedral structure involving the 3 hydroxamic acid groups. Mol. modeling showed it to have similar features to other ferric trihydroxamic siderophores whose 3-dimensional structures have been established. The mol. was shown to have little flexibility around the **Fe** chelation center, although the terminal (Orn-3) residue, which was not involved in **Fe** binding except at its δN atom, had more motional freedom.

CC 10-1 (Microbial, Algal, and Fungal Biochemistry)

IT **7439-89-6**, Iron, properties
RL: PRP (Properties)
(coordination of iron in exochelin MS from Mycobacterium smegmatis)

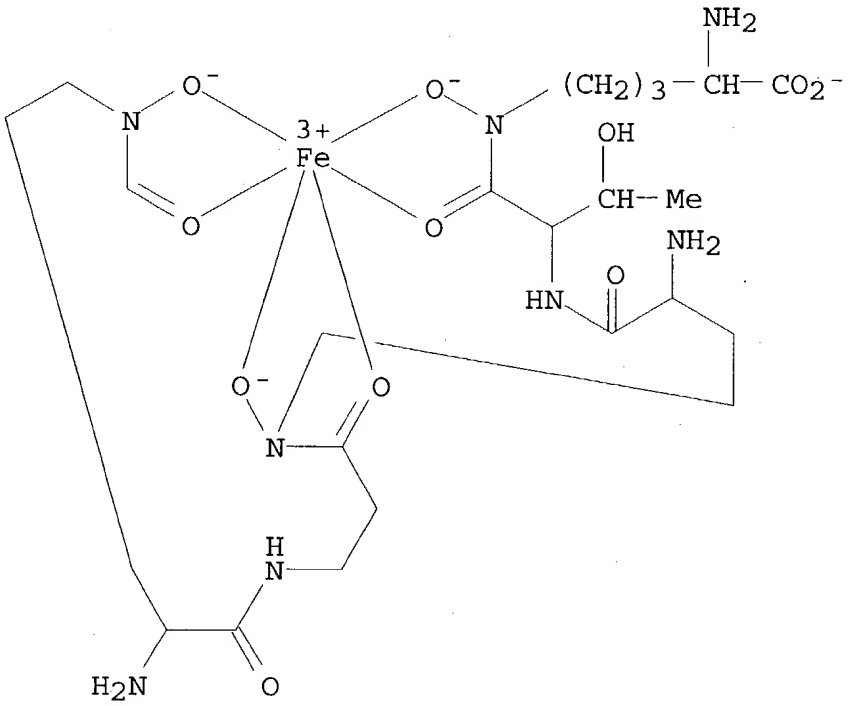
IT **162382-31-2P**, Exochelin MS
RL: PRP (Properties); PUR (Purification or recovery); RCT (Reactant); PREP

(Preparation); RACT (Reactant or reagent)
(isolation, purification, and structure of exochelin MS, the extracellular
siderophore from Mycobacterium smegmatis)
IT **161834-86-2P**, Deferri-exochelin MS
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(isolation, purification, and structure of exochelin MS, the extracellular
siderophore from Mycobacterium smegmatis)
IT **161834-86-2P**, Deferri-exochelin MS
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(isolation, purification, and structure of exochelin MS, the extracellular
siderophore from Mycobacterium smegmatis)
IT **7439-89-6**, Iron, properties
RL: PRP (Properties)
(coordination of iron in exochelin MS from Mycobacterium smegmatis)
RN 7439-89-6 HCAPLUS
CN Iron (7CI, 8CI, 9CI) (CA INDEX NAME)

Fe

IT **162382-31-2P**, Exochelin MS
RL: PRP (Properties); PUR (Purification or recovery); RCT (Reactant); PREP
(Preparation); RACT (Reactant or reagent)
(isolation, purification, and structure of exochelin MS, the extracellular
siderophore from Mycobacterium smegmatis)
RN 162382-31-2 HCAPLUS
CN Ferrate(1-), [N5-[N-[N5-[N-[N5-(formyl-κO)-N5-(hydroxy-κO)-D-ornithyl-κO1]-β-alanyl]-N5-(hydroxy-κO)-D-ornithyl]-D-allothreonyl-κO1]-N5-(hydroxy-κO)-L-ornithinato(4-)]-, hydrogen (9CI) (CA INDEX NAME)

PAGE 1-A



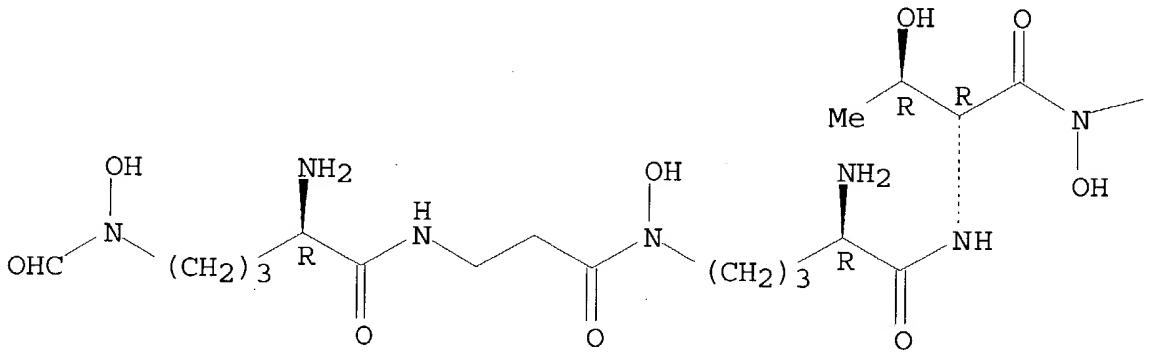
PAGE 2-A

● H^+

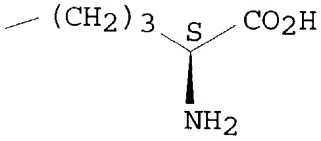
IT **161834-86-2P**, Deferri-exochelin MS
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(isolation, purification, and structure of exochelin MS, the extracellular
siderophore from Mycobacterium smegmatis)
RN 161834-86-2 HCAPLUS
CN L-Ornithine,
N5-[N-[N5-[N-(N5-formyl-N5-hydroxy-D-ornithyl)-β-alanyl]-
N5-hydroxy-D-ornithyl]-D-allothreonyl]-N5-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L12 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1987:117980 HCAPLUS
DOCUMENT NUMBER: 106:117980
TITLE: Inactivation of enzymes and oxidative modification of proteins by stimulated neutrophils
AUTHOR(S): Oliver, Cynthia N.
CORPORATE SOURCE: Lab. Biochem., Natl. Heart, Lung, Blood Inst., Bethesda, MD, 20892, USA
SOURCE: Archives of Biochemistry and Biophysics (1987), 253(1), 62-72
CODEN: ABBIA4; ISSN: 0003-9861
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Differentiated, stimulated HL-60 cells and freshly isolated, stimulated neutrophils inactivate glutamine synthetase (EC 6.3.1.2) either inside or outside of Escherichia coli. Although the reaction occurs in the absence of **Fe**(III), it is stimulated by added **Fe**(III).

Inactivation required mol. O and is partially inhibited by Mn(II), catalase, superoxide dismutase, and metal chelators, EDTA and o-phenanthroline. Both the kinetics and the extent of glutamine synthetase inactivation differ when neutrophils are stimulated with phorbol esters compared with **formylated peptides**. Glutamine synthetase inactivation catalyzed by mixed-function oxidation (MFO) systems is accompanied by the formation of protein carbonyl derivs. which form stable hydrazones when treated with 2,4-dinitrophenylhydrazine. Multiple carbonyl derivs. are formed in the soluble protein fraction of stimulated neutrophils and these derivs. collectively exhibit an absorbance spectrum similar to that of glutamine synthetase inactivated by liver microsomal cytochrome P 450 MFO system (K. Nakamura, et al., 1985). These observations are related to the microbicidal action of neutrophils.

CC 15-10 (Immunochemistry)
Section cross-reference(s): 7

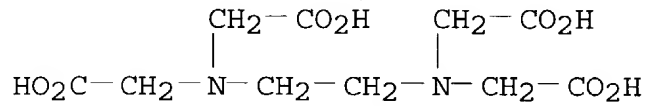
IT **60-00-4**, Ethylene diaminetetraacetic acid, biological studies **7439-96-5**, biological studies **9054-89-1**, Superoxide dismutase
RL: BIOL (Biological study)
(enzyme inactivation by stimulated human neutrophil response to)

IT **66-71-7**, o-Phenanthroline **7439-89-6**, biological studies **7782-44-7**, Oxygen, biological studies **9001-05-2**, Catalase
RL: BIOL (Biological study)
(enzyme inactivation by stimulated human neutrophil response to)

IT **9001-50-7**, Glyceraldehyde 3-phosphate dehydrogenase **9001-59-6**, Pyruvate kinase **9001-60-9**, Lactate dehydrogenase **9001-83-6**, Phosphoglycerate kinase **9023-70-5**, Glutamine synthetase
RL: BIOL (Biological study)
(inactivation of, by stimulated neutrophil, of human, microbicidal action in relation to)

IT **60-00-4**, Ethylene diaminetetraacetic acid, biological studies **7439-96-5**, biological studies **9054-89-1**, Superoxide dismutase
RL: BIOL (Biological study)
(enzyme inactivation by stimulated human neutrophil response to)

RN 60-00-4 HCAPLUS
CN Glycine, N,N'-1,2-ethanediylbis[N-(carboxymethyl)- (9CI) (CA INDEX NAME)

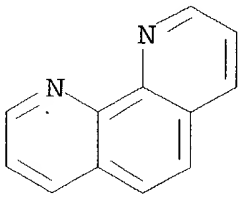


RN 7439-96-5 HCAPLUS
CN Manganese (8CI, 9CI) (CA INDEX NAME)

Mn

RN 9054-89-1 HCAPLUS
CN Dismutase, superoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **66-71-7**, o-Phenanthroline **7439-89-6**, biological studies **7782-44-7**, Oxygen, biological studies **9001-05-2**, Catalase
RL: BIOL (Biological study)
(enzyme inactivation by stimulated human neutrophil response to)
RN 66-71-7 HCAPLUS
CN 1,10-Phenanthroline (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 7439-89-6 HCAPLUS
CN Iron (7CI, 8CI, 9CI) (CA INDEX NAME)

Fe

RN 7782-44-7 HCAPLUS
CN Oxygen (8CI, 9CI) (CA INDEX NAME)

O=O

RN 9001-05-2 HCAPLUS
CN Catalase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **9001-50-7**, Glyceraldehyde 3-phosphate dehydrogenase
9001-59-6, Pyruvate kinase **9001-60-9**, Lactate
dehydrogenase **9001-83-6**, Phosphoglycerate kinase
9023-70-5, Glutamine synthetase
RL: BIOL (Biological study)
(inactivation of, by stimulated neutrophil, of human, microbicidal
action in relation to)
RN 9001-50-7 HCAPLUS
CN Dehydrogenase, glyceraldehyde phosphate (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9001-59-6 HCAPLUS
CN Kinase (phosphorylating), pyruvate (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9001-60-9 HCAPLUS
CN Dehydrogenase, lactate (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9001-83-6 HCAPLUS
CN Kinase (phosphorylating), phosphoglycerate (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9023-70-5 HCAPLUS
CN Synthetase, glutamine (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

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potatoes. The polysaccharide synthesized by muscle phosphorylase resembles the amylose fraction of natural starch (7), while the enzymes from the other mammalian tissues (8) and from yeast (9) form a polysaccharide which resembles glycogen. Potato phosphorylase synthesizes a polysaccharide which resembles amylose (10). Cori and Cori (11) showed that phosphorylases of mammalian origin require the presence of polysaccharide for polysaccharide synthesis, and this was confirmed by Hanes (12) for plant phosphorylase. His claim that maltose could be substituted for polysaccharide was not confirmed by Green and Stumpf (13) nor by work done in this laboratory, when care was taken to free the maltose of polysaccharide impurities. Cori, Colowick, and Cori (14) found that phosphorylases derived from vertebrate tissues required the addition of adenylic acid as coenzyme, while yeast (9) and potato (13) phosphorylases were shown to be active in the absence of added adenylic acid. Reducing agents (glutathione, cysteine, KCN) were shown to increase the activity of muscle phosphorylase (15), while they are without effect on potato phosphorylase (13). The crystallization of muscle phosphorylase was announced in
a preliminary note (16). The present paper deals with the method of preparation of the crystalline enzyme and some of its properties.

L2 ANSWER 2 OF 44 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
TI On a class of elliptic problems in R-2: symmetry and uniqueness results
AB In the plane R-2, we classify all solutions for an elliptic problem of Liouville type involving a (radial) weight function. As a consequence, we clarify the origin of the non-radially symmetric solutions for the given problem, as established by Chanillo and **Kiessling**.
For a more general class of Liouville-type problems, we show that, rather than radial symmetry, the solutions always inherit the invariance, of the problem under inversion with respect to suitable circles. This symmetry result is derived with the help of a 'shrinking-sphere' method.

L2 ANSWER 3 OF 44 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI Change of ultraviolet absorbance of sunscreens by exposure to solar-simulated radiation.
CO Laboratoires garnier (France); **E kiessling and cie gmbh (Germany)** ; Bayer (Germany); Roche Posay (France); Beiersdorf (Germany); Tiroler nussol sonnenkosmetik (Germany); P and g (United Kingdom); Sara Lee (Germany); Vichy Farmacosmetici (France); Johnson and Johnson (Germany); Bubchen werk ewald hermes pharmazeutische fabrik gmbh (Germany)

L2 ANSWER 4 OF 44 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
TI Zeros of wave functions in Ginzburg-Landau model for small epsilon
AB In this paper we study zeros of condensate wave functions in Ginzburg-Landau model. The main question we are concerned with is when a condensate wave function appears to have only isolated zeros of degree one. Our main result shows that under some conditions on the energy and the tension field a condensate wave function will appear to possess only the expected number of isolated zeros of degree one. We will also discuss how the heat Bow can deform a condensate wave function and make it appear to possess the expected number of isolated zeros of degree one. In the end we will mention a slight improvement of a uniqueness result of Chanillo and **Kiessling**.

L2 ANSWER 5 OF 44 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
TI Johann **Kiessling**, the Krakatoa event and the development of atmospheric optics after 1883
TI Johann **Kiessling**, the Krakatoa event and the development of atmospheric optics after 1883

L2 ANSWER 6 OF 44 MEDLINE on STN DUPLICATE 1
TI Escape mechanisms in tumor immunity: a year 2000 update.

AB The current consensus of opinion has it that most or possibly all tumors, spontaneous as well as induced, are immunogenic, expressing antigens in a form recognizable by the host immune system. Accordingly, in order to progress, tumors have to evolve strategies for evading immune responses. The purpose of this review is to consider the current status of knowledge concerning these different tumor escape strategies. It represents an update of an article originally published in this journal in 1997 (Pawelec, Zeuthen, and **Kiessling**, 1997). Therefore, it focuses mostly on publications that have appeared since then, illustrating the impressive accumulation of new data since that time and the importance currently attributed to studies of tumor escape from the immune response.

L2 ANSWER 7 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI The 2000 Horace S. Isbell award
AB Laura L. **Kiessling** is the recipient of the Horace S. Isbell Award 2000. The award is in recognition of the accomplishments of carbohydrate scientists who have not yet reached their 41st birthday. **Kiessling**'s research focuses on elucidating and exploiting the mechanisms of cell surface recognition processes, especially those that involve protein-saccharide recognition and oligosaccharide function.
ST award **Kiessling**
IT Awards
(Horace S. Isbell Award; Laura L. **Kiessling** received the Horace S. Isbell Award 2000)

L2 ANSWER 8 OF 44 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
TI **Kiessling:** Seeing connections
TI **Kiessling:** Seeing connections

L2 ANSWER 9 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI Arthur C. Cope Scholars
AB Laura L. **Kiessling** received the Arthur C. Cope Scholars award for her achievements in organic chemical and biochem.
ST **Kiessling** Arthur Cope Scholar award biochem

L2 ANSWER 10 OF 44 MEDLINE on STN DUPLICATE 2
TI Structural changes in subdomain 2 of G-actin observed by fluorescence spectroscopy.
AB The influence of DNase I binding to Ca-ATP-G-actin and of Ca2+/Mg2+ and ATP/ADP exchange on the conformation of G-actin were investigated by measuring the fluorescence of dansyl cadaverine (DC) conjugated to Gln41 in subdomain 2 of the protein. Fluorescence resonance energy transfer (FRET) between this probe and N-[4-(dimethylamino)-3,5-dinitrophenyl]maleimide (DDPM) attached to Cys374 in subdomain 1 was also measured. Contrary to an earlier report [dos Remedios, **Kiessling** and Hambly (1994) in Synchrotron Radiation in the Biosciences (Chance, B., Deisenhofer, J., Ebashi, S., Goodhead, D. T., Helliwell, J. R., Huxley, H. E., Iizuka, T., Kirz, J., Mitsui, T., Rubenstein, E. et al., eds.), pp. 418-425, Oxford University Press, Oxford], the distance between these probes did not change significantly when DNase I was bound to actin. A small but reproducible increase in the quantum yield and a blue shift of the DC fluorescence maximum were observed when bound Ca2+ was replaced by Mg2+. A large increase (about 70%) in the quantum yield and an approx. 12 nm blue shift of the emission spectrum occurred when ATP in Mg-G-actin was replaced by ADP. These changes were not accompanied by any significant change in the FRET distance between the dansyl donor and DDPM acceptor probes. A substantial change in the fluorescence of DC-actin was observed after proteolytic removal of the last three residues of actin, in accordance with earlier evidence suggesting that there is a conformational coupling between subdomain 2 and the C-terminal segment in subdomain 1 of actin. The results are discussed in relation to recently published data obtained with another fluorescent probe and to earlier observations based on limited cleavage using proteolytic enzymes.

L2 ANSWER 11 OF 44 MEDLINE on STN DUPLICATE 3
TI Preliminary studies on the use of an ABR amplitude projection procedure for hearing aid selection.
AB Hearing aid selection in young nonverbal children is difficult and objective selection procedures are needed. **Kiessling** (Scand Audiol 1982;11:269-275; Arch Otorhinolaryngol 1983;238:233-240) has proposed an objective hearing aid selection method based on an unaided ABR amplitude projection procedure. However, **Kiessling**'s ABR projection method is based on the assumption that ABR amplitude is directly related to the loudness of a signal--an assumption which has not been tested. This assumption was investigated in a group of ten normally hearing and three hearing-impaired listeners. The results indicated that ABR amplitude measures obtained in a single trial do not always correlate well with perceived loudness, but ABR amplitudes averaged over several trials do correlate well with estimates of perceived loudness. The hearing-impaired listeners then participated in a second phase of the investigation in which hearing aids chosen by the ABR projection procedure were compared with hearing aids chosen by more conventional methods. The results indicated that the projection procedure prescribed appropriate gain and compression characteristics for two of the three hearing-impaired listeners.

L2 ANSWER 12 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI Further investigations of the type II Diels-Alder route to the bicyclic core of esperamicin/calichemicin reveal a regiochemical misassignment: meta versus para selectivity
AB The intramol. Diels-Alder reaction of 4-MeOC6H4(CH2)nOCH:CHC(:CH2)CH(OSiMe2CMe3)C.tplbond.CCH:CHC.tplbond.CCH:CHCO2Me (n = 0, 1) gave the adduct I, not II as previously reported (S. L. Schreiber, L. L. **Kiessling**, 1988).

L2 ANSWER 13 OF 44 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI [Is brain biopsy now obsolete?].
HIRNBIOPSIE OBSOLET?.
AB In the following series of articles, the 'pros and cons' of brain biopsies will be presented from a neuropathological point of view. Achievements in modern clinical imaging techniques (CT, MR, ultrasound) have thus far failed to significantly reduce the average rate of diagnostic failures throughout several decades although the spectrum of underrated diseases has changed. Some remaining indications for a brain biopsy in case of tumors (**Kiessling** et al., 1988), metabolic disorders (Pfeiffer, 1988), and inflammatory processes (Schroder, 1988) are discussed.

L2 ANSWER 14 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI Balance of distribution of some transition metals between the (M', M'')B and (M', M'')2B phases
AB A study was made of the preferential distribution between the phases (M', M'')2B and (M', M'')B present in the 2-phase fields of the M'-M''-B systems for the transition metals with atomic nos. 24-28. The metal with the smaller atomic number is systematically concentrated in the phase richer in B. The extreme values of the distribution ratio α°, calculated according to Haegg and **Kiessling** (1952-53) at 1073-1473 K, diminish progressively in relation to the increase in the difference between the atomic nos. of the metallic atoms. Further, α° increases gradually as the temperature increases. The preferential distribution was justified considering the different metal-nonmetal affinity, and recalling analogous considerations expressed in relation to nitrides, carbides, and hydrides of transition metals.

L2 ANSWER 15 OF 44 MEDLINE on STN DUPLICATE 4

TI Enhanced natural killer (NK) cell activity and NK-sensitive thymic cells in murine muscular dystrophy.

AB Studies have shown that there is an abnormality in the thymus of dystrophic mice with respect to age-dependent thymus weight changes and altered morphology (T. DeKretser and B. Livett, Nature (London) 263, 682, 1976). Recently, others have shown that natural killer (NK) cells can lyse cells of a large, immature, rapidly dividing cell subpopulation within the thymus of normal young (3 weeks of age) mice (M. Hansson, K. Karre, R. **Kiessling**, J. Roder, B. Anderson, and P. Hayry, J. Immunol. 123, 765, 1979). The NK susceptibility of dystrophic mouse thymocytes as targets was therefore studied. Spleen cells from normal (+/+) and dystrophic (dy2J/dy2J) male C57BL/6J mice 8-10 weeks old were passed over nylon wool and the nonadherent cells were incubated with 51Cr-labeled YAC-1 lymphoma target cells or thymocytes in a 51Cr-release assay. Spleen cells from dystrophic mice killed twofold more YAC-1 target cells than did spleen cells from normal mice. Thymocytes from 3- to 4-week-old dystrophic mice were three to four times more susceptible to NK lysis by dystrophic mouse spleen cells as compared with normal mouse spleen cells. Spleen cells from dystrophic mice had the same NK activity against dystrophic and normal mouse thymocytes as targets. Normal mouse spleen cells killed three- to fourfold more dystrophic mouse thymocytes than that of normal mouse thymocytes as targets. Target cell-binding studies revealed that conjugate-forming cells from nylon nonadherent dystrophic mouse spleen cells were found to be two- to fourfold greater than for normal mouse spleen cells using YAC-1 tumor cells as targets. The number of lymphocytes bound per YAC-1 target cell ranged from 2 to 5 for dystrophic mouse spleen cells as compared with 1 to 2 for the normal control group. Using both normal and dystrophic mouse thymocytes as targets, the conjugate-forming cells from dystrophic mouse spleen cells were also found to be twofold greater than in the normal control group. Cold target inhibition studies revealed that the natural killing of dystrophic mouse thymocytes was due to a YAC-1-reactive NK cell. Effector cell depletion studies using monoclonal anti-Thy-1.2 plus complement treatment and plastic petri dish adherence also revealed that the natural killing of dystrophic mouse thymocytes was not due to either T lymphocytes or macrophages. Taken together, these results show an increase in NK-sensitive thymocyte targets in dystrophic mice, in combination with an increase in splenic NK activity.

L2 ANSWER 16 OF 44 MEDLINE on STN DUPLICATE 5

TI Thymus independence of hybrid resistance against a panel of T-cell lymphomas of H-2b origin.

AB Adult thymectomy, followed by whole-body irradiation and reconstitution with fetal liver, was performed to study the T-cell dependence of F1 hybrid resistance to a panel of lymphomas of H-2b origin. Previously, the pattern of hybrid resistance against the same lymphomas was found to correlate with the pattern of NK-activity in a spectrum of F1 hybrids (**Kiessling** et al., 1975). We now show that hybrid resistance against three lymphomas of C57BL/6 origin, P-52-127-166, RBL-5 and EL-4 and against YLD, of C57L origin, is expressed in the absence of thymus. In another series of experiments, the effectors responsible for hybrid resistance to the transplanted lymphoma EL-4 were studied by reconstituting thymectomized and non-thymectomized C57BL mice with syngeneic bone marrow from NK-deficient beige mutant or wild-type C57BL donors. While the recipients of beige bone marrow had a clearly reduced tumor resistance, thymectomy did not decrease resistance further. This study supports the hypothesis that resistance to these lymphomas in F1 hybrids as well as in syngeneic mice is mainly mediated by natural killer cells.

L2 ANSWER 17 OF 44 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

TI **KIESSLING,** ROLAND IN A STEEL DIALOG WITH HIMSELF

TI **KIESSLING,** ROLAND IN A STEEL DIALOG WITH HIMSELF

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TI Contemporary topics in immunobiology.

AB This present volume reflects both several of the more classical areas of immunology now addressed in the light of contemporary immunology, and several newer directions that have been taken in other fields. The general subject of T-cell heterogeneity and functions of T-cell subpopulations is addressed in Chapters 1 and 2. The potential role of genes of the major histocompatibility complex in controlling the immune functions of T lymphocytes still remains a major unresolved issue in immunogenetics, and the current status of this problem is excellently reviewed by J.F.A.P.Miller. The further elucidation of functional subpopulations of human T lymphocytes has been particularly hampered by the lack of available markers for characterizing and isolating such subpopulations. A major step in this direction has been made by L. Moretta, M. Ferrarine, and M.D. Cooper, who review their experience with Fc-receptor-bearing human T-lymphocyte populations. Although the predominant interest in lymphocyte subpopulations has centered on the T-cell series, the subject of B-cell heterogeneity has become a considerably escalating field of research in immunobiology, in part through studies of the role or roles of membrane immunoglobulins as antigen receptors for immunity or tolerance. Progress in this field has also been considerably aided by the discoveries of murine IgD and allotypes of murine IgM and IgD, and these aspects are extensively covered by J.W. Goding in Chapter 7 and J.F. Kearney and E.R. Abney in Chapter 8. Of considerable current interest in many areas of the world is the potential benefit to be gained from a better understanding of the role of the immune response in protection against parasitic infections. This field desperately requires the application of 'newer' immunobiological approaches and one facet of this, namely, studies with athymic nude mice, is well reviewed in Chapter 3 by G.F. Mitchell. The remaining three chapters of this volume are devoted to the field of tumor immunology and reflect the still considerable uncertainty of the relative roles played by various cell types in immune responses to different tumor antigens. In addition to the anti-tumor response of T cells, B cells, and macrophages, a new cell type - termed the natural killer cell - has recently been recognized as another potential cell type that may be capable of lysing many tumor cell lines. In Chapter killer R. **Kiessling** and O. Haller comprehensively and O.Haller compreshensively review the evidence that these natural liller cells may play a major role in immunological surveillance. On a broader level, J.S. Haskill, P. Hayry, and L.A. Radov P.Hayry, and L.A.Radow have considered the potential role of various cell types in allogeneic and anti-tumor immunity, but have particularly concentrated in Chapter 5 on a major aspect that is frequently overlooked and ill defined, namely the in situ tumor response, as contrasted with systemic immunity. The analysis of mechanisms of T-cell-mediated immunity to tumors is relatively difficult to assess in vivo studies; as in many other systems, considerable efforts have been made to develop primary immune responses in vitro, and the experience in this field R.C. Burton, S.E. Chism, and N.L. Warner S.E.Chism, and N.L.Warner is reviewed in Chapter 4, with particular emphasis on the potential to further analyze the nature of tumor antigens as recognized by T lymphocytes.

L2 ANSWER 19 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN

TI Preparation of 2-DL-phosphoglyceric acid- a substrate of the enzyme enolase

AB 2-DL-Phosphoglyceric acid prepared according to the method of **Kiessling** (1953) was further purified by a filtration through a column of Dowex 50-X4 (Na+), using water as eluent. The purity of the resulting preparation was 70%.

L2 ANSWER 20 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN

TI Formation and growth of oxide inclusions in austenitic chromium-nickel steel

AB For the deoxidn. of 18/8 Cr-Ni steel commonly Mn and Si are applied, which form by the reaction: eskolaite (Cr_2O_3), $MnCr_2O_4$, $MnSiO_3$, SiO_2 glass, Mn silicate, and Mn-Cr silicate glasses, as typical inclusions in the steel ingots. Well-crystallized eskolaite is the principal inclusion phase in 18/8 Cr-Ni steels containing <10% Mn and <0.19% Si. With increasing Si addition, the appearance of SiO_2 glass as inclusions is observed rather abruptly, $MnCr_2O_4$ is evident for Mn-richer steels, and/or a Cr_2O_3 containing rhodonite. In the system MnO-Cr_2O_3-SiO_2 (**Kiessling** and Lange, 1964) the composition of individual inclusions is plotted chiefly in the partial field MnO-Cr_2O_3-SiO_2-$MnCr_2O_4$. When addnl. Al is used for deoxidn. (the Mn-Si deoxidn. occurs in the 1st step of the reactions), corundum is the dominant inclusion in the ingots, together, more or less regularly, with a highly viscous Al silicate glass. Furthermore there are observed crystalline solns. of $MnCr_2O_4$ with galaxite, $MnAl_2O_4$, e.g., a phase with a0 = 8.37 A., and combined with Al silicate glass. Introduction of Ti for deoxidn., together with Mn and Si, brings about inclusions of Mn titanate (presumably Mn_2TiO_4), anosovite (Ti_3O_5), and most characteristically, with TiN (presumably in crystalline solution with TiC and TiO). Deoxidn. with Ca (or its alloys) in combination with Mn, Si, and Al brings about Ca silicate glasses and crystalline phases of the system CaO-Al_2O_3-SiO_2. Special observations are discussed on the growth phenomena of different crystalline inclusion phases, their intergrowths, also the coagulation of glass droplets and the like, also intergrowths of TiN with oxides (or Ca aluminates). Larger aggregates of this type may easily cause defects in the steel.

L2 ANSWER 21 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN

TI Oxidation of DL-α-glycerophosphate and β-hydroxybutyrate in red and white skeletal muscle

ST SKELETAL MUSCLE OXIDN PYRUVATE; PYRUVATE OXIDN SKELETAL MUSCLE; GLYCEROPHOSPHATE OXIDN SKELETAL MUSCLE; HYDROXYBUTYRATE OXIDN SKELETAL MUSCLE; RED MUSCLE PYRUVATE OXIDN; WHITE MUSCLE PYRUVATE OXIDN; MUSCLE PYRUVATE OXIDN; LUNDQUIST C G; **KIESSLING** K H

L2 ANSWER 22 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN

TI Effect of acute and chronic ethanol ingestion on rat liver ATP

AB The rat liver concentration of ATP increased almost 100% 8 hrs. after the incubation of EtOH (6 g./kg.) but returned to control levels after 24 hrs. This effect was not sex dependent. When male rats were fed EtOH for 2 months or longer, the liver ATP decreased. This decrease persisted for as long as 16 months, but returned to control levels within 2 days after the EtOH was withdrawn. These results of the chronic administration EtOH were found only with male rats and could be duplicated by chronic feeding of AcH. The increase in hepatic ATP during acute EtOH intoxication may have resulted from electron transport from cytoplasmic NADH to the mitochondrial cytochrome system, while the decrease in ATP after chronic EtOH ingestion was probably due to degenerative changes in the mitochondrial structure. The fact that females are spared the effect of ATP depression during the chronic administration of EtOH may be correlated with the failure of EtOH to suppress the liver mitochondrial oxidation of succinate in females (**Kiessling** and Tilander, CA 59, 10657c). 18 references.

L2 ANSWER 23 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN

TI System manganese-boron

AB Briquetted mixts. of electrolytic 99.5% Mn and refined 98.5% B were roasted at 900-1350° in an Ar atmospheric The compds., Mn_2B, MnB, Mn_3B_4 (**Kiessling**, CA 44, 6754i), and MnB_2 (Aronsson, CA 58, 10697b), were easily synthesized, only Mn_4B (K., loc. cit.) could not be obtained in

pure state. Also, Mn borides, obtained by electrolysis of the melts (Aleonard, CA 55, 14124e) could not be synthesized from elements by pressing up to 2000°. Besides the individual compds., roasts of intermediate composition were also prepared The phase diagram of the system shows the probability of formation of a compound with >66.7% B. The Mn borides are easily soluble in HCl. The rate of dissoln. and the amount of boranes formed decrease and the resistance to chemical agents (O,N,NH3) and the m.p. increase with increasing proportion of B in the borides. Mn and B nitrides are formed at 500-1300° by the action of NH3 on Mn2B and MnB and at 700° by that of N on Mn2B; Mn2B forms carbides with graphite powder at 1500°, while borides with higher B contents do not react with N and NH3 at 1300° and with graphite at 1800°. However, at high temps., in the presence of C and, in some cases, also of NH3, all Mn borides are transformed into MnB. 17 references.

L2 ANSWER 24 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN

TI Kinetics and mechanism of hydrolysis of dihydroxyacetone phosphate. II. Hydrolysis in a strongly alkaline medium

AB cf. CA 59, 1448d. The hydrolysis of HOCH2COCH2OPO3H2 (I) was carried out in aqueous solns. of KOH at 0 and 25°, with I concentration of approx. 0.001 mole; the KOH concns. varied from 0.008 to 0.7 mole. Addns. of KCl were made to KOH solns. to maintain the same ionic strength. Test samples were poured into 1 ml. M H2SO4 solution to stop the hydrolysis, and inorg. phosphate concentration of the solution was determined colorimetrically. The rate of I hydrolysis increased with increase of KOH concentration up to 0.5 mole/l., and remained the same at higher KOH concns. A slight increase in hydrolysis rate was observed on increasing KCl concentration At the same KOH concentration, addition of 0.05 mole/l. glycine or of 0.001 mole/l. MgSO4 considerably retarded reaction, the former addition halving the hydrolysis rate. Addition of Na thioglycolate had a similar effect, but determination was colorimetrically difficult. Temperature increase from 0 to 25° considerably increased I hydrolysis in alkaline media. To investigate the route of lactic acid formation in alkaline hydrolysis of I (**Kiessling**, CA 28, 47018), paper chromatography of the products with 10:10:3 BuOH-water-HCO2H was used. Neither dihydroxyacetone nor methylglyoxal was detected, but in the case of the latter the method was not conclusive. Extraction with Et2O of the hydrolysis product of 0.064 mole/l. I and 0.3 mole/l. KOH was carried out in a continuous apparatus at 0°. The residue after Et2O evaporation was dissolved in a little H2O, and to this solution a saturated solution of 2,4-dinitrophenylhydrazine in 2N HCl was added at 30°. Retarding effect on I hydrolysis by nucleophilic agents indicated that the OH ion attached to the carbonyl group. A reaction mechanism was proposed for the conversion of I to methylglyoxal in alkaline media.

L2 ANSWER 25 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN

TI Crystal structure of RuB2, OsB2, and IrB1.35 and some general comments on the crystal chemistry of borides in the composition range Me-B to MeB3

AB cf. CA 57, 9312c. Details are given of chemical and x-ray analyses of the title compds. previously reported (loc. cit.). Results for RuB2 and OsB2 are in good agreement with those of Roof and Kempter (CA 57, 14518f). The space group C2/m was assigned to IrB1.35 (previously given as IrB1.5) and the following monoclinic lattice parameters were found: a 10.525, b 2.910, c 6.099 A., β 91°4'. The structure of the borides containing 50-75 atomic-% B consists of alternate layers of close-packed metal atoms and of B stacked in the c direction. The spacing of the B atoms is determined by the metallic radius (**Kiessling**, CA 42, 5738d). With increasing metallic radius, the B-metal distances decrease while the B-B distances increase. In IrB1.35 the B atoms are sym. located although only 70% of the available sites are occupied.

L2 ANSWER 26 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI The crystal structure of Cr3B4
AB Alloys prepared by the are melting of mixts. of B and Cr in an Ar atmospheric were photographed by x-ray with a Guinier camera and atomic parameters were determined in a Weissenberg camera with Mo Kα radiation. No lattice-parameter variations were observed. In Cr3B4 there are no abnormally short B-B interat. distances as suggested by **Kiessling** (CA 44, 9850g).

L2 ANSWER 27 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI The systems: V-B, Nb-B, V-B-Si, and Ta-B-Si
AB cf. C.A. 51, 12723g. X-ray measurements were made of samples in the binary systems V-B and Nb-B and in the quasi-binary cuts Ta2B-Ta2Si and V5Si3-V5B3. The metals were treated with H to facilitate powdering, then tempered in A. The samples for the binary systems were tempered by hot-pressing (12 hrs. at 1600° or 2000° in A). The samples in the V-B-Si system were cold pressed and sintered in A (24 hrs., 1450°); in the Ta-Si-B system they were cold pressed in H then heated 12 hrs. at 1900°. A new phase of about 30% B, corresponding to approx. composition V2B, was found which is an isotype of the corresponding phases in the Nb-B and Ta-B systems. The β' phase reported in Nb-B (Andersson and **Kiessling**, C.A. 44, 6713h) was identified as NbO. The 2 phases in the cut Ta2Si-Ta2B exhibited slight solubility in each other. Addition of 20 mol. % Ta2Si to Ta2B gave a stabilized phase. A ternary phase with T 2 structure (composition V5SiB2) was found, analogous to the T 2 phase, Mo5(Si,B)3 (loc. cit.). Evaluation by powder diagrams with CrKα radiation of the T 2 structure (D184h) gave lattice consts. a = 5.80 kX, c = 10.77. To summarize results on the M5(Si,B)3 phases, the stability regions of the T 1, T 2, and D88 phases of the boride-silicides of metals of Group IVA, VA, and VIA elements were compared. The lattice constant of Nb5Si3 previously reported (C.A. 51, 924f) should be a = 6.557 instead of a = 6.777.

L2 ANSWER 28 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI A new synthesis of 2-phosphoryl-D-glyceric acid
AB A definite synthesis of D-HOCH2CH(OPO2H2)CO2H (I) is described which yields the pure compound in quantity as the crystalline tri-Na salt (II). Although the rotation of this synthetic material is in disagreement with that of previously reported prepns. of I (cf. Meyerhof and **Kiessling**, C.A. 29, 3453.7), chemical and enzymic studies have given conclusive proof of the identity and purity of this preparation D-Galactose (III) (100 g.) stirred 18 hrs. with 8 l. Me2CO containing 80 cc. concentrated H2SO4, the mixture cooled, the acid neutralized with gaseous NH3, the precipitate filtered off, the filtrate concentrated, the residue dissolved in 1 l. CHCl3, the solution washed with 100 cc. H2O and evaporated, and the residue distilled yielded 100-10 g. (70%) 1,2:3,4-di-O-isopropylidene-D-galactopyranose (IV), b0.1-0.2 110-20°. IV (110 g.) stirred 5 hrs. at 100° with 100 cc. PhMe, 100 cc. PhCH2Cl, and 150 g. powdered KOH, the mixture cooled to room temperature, diluted with 250 cc. ice water, and stirred until the salts dissolved, the organic layer washed 3 times with H2O and evaporated, and the residue distilled yielded 140 g. (95%) 6-O-Bz derivative (V) of IV, b0.01 130-60°. V (140 g.) dissolved in 500 cc. dry MeOH containing 2% HCl, the solution refluxed 3 hrs., cooled, stirred with 35 g. Ag2O until neutral, and filtered through Filter-Cel, the alc. filtrate treated with H2S to remove a trace of Ag ion, filtered again through Filter-Cel, and evaporated to dryness in vacuo, the crystalline residue dissolved in 150-200 cc. hot absolute EtOH, the solution cooled overnight to 5°, the crystalline deposit washed color-free with a little cold absolute EtOH and dissolved in 200 cc. absolute

EtOH, and the solution treated with C, filtered, and cooled deposited 40 g. almost pure Me 6-O-benzyl-α-D-galactopyranoside (VI), m. 142-4°; the alc. mother liquor evaporated in vacuo, the residue treated with alc. HCl, and the mixture worked up in the same manner as the main fraction yielded a 2nd crop of 30 g. V; a 3rd treatment of the mother liquor gave an addnl. 10 g. V to bring the total yield to 80 g. (70%); the V recrystd. several times from absolute EtOH and dried at 50° and 0.1 mm. over P2O5 gave an analytical sample, m. 144-5°, [α]D 113° (c 3, H2O). Pure V consumed 2 moles NaIO4/mole, and on catalytic debenzylation was converted to Me α-D-galactopyranoside, m. 102-5°, [α]D 180 (c 2, H2O). V (20 g.) added to 40 g. NaIO4 in 300 cc. cold H2O, the solution let stand overnight at room temperature and extracted with four 400-cc. portions Et2O, the extract poured into a 2-l. flask containing 100 cc. H2O, and the Et2O distilled off at 35° bath temperature gave an aqueous solution of the dialdehyde, [α]D 82.5°, which had an oxidation equivalent of 64.4; the dialdehyde solution diluted to about 400 cc. with H2O, treated with 56 g. iodine and 70 g. KI in 50 cc. H2O followed immediately by 65 g. K2CO3 and 48 g. KHCO3 in 500 cc. H2O, the mixture left 2 hrs. in the dark at room temperature with occasional shaking, treated cautiously in a large pan with 142 cc. 10N H2SO4, the excess iodine reduced with 40-50 g. Na2S2O3, the clear solution filtered through cotton to remove a small amount of dark oil and extracted with four 1-l. portions Et2O, the extract mixed with 100 cc. H2O, the Et2O removed at 50° in vacuo, the residual aqueous solution of the dicarboxylic acid having [α]D 14.6°, heated 2 hrs. on the steam bath, cooled, and extracted with four 100-cc. portions Et2O, the extract dried with Na2SO4 and concentrated in vacuo at 50°, the residual sirup dissolved in 50 cc. H2O, the solution again evaporated, the resulting sirup (12 g.) dissolved in 120 cc. H2O, the solution treated with 3 g. powdered Ca(OH)2, the mixture slowly warmed over a bunsen burner, finally heated to boiling, and filtered rapidly while hot, the filtrate cooled several hrs. at 5°, and the crystalline deposit recrystd. from 110 cc. hot H2O gave 9.5 g. (60%) pure C 3-O-benzyl-D-glycerate, D-[PhCH2OCH2CH(OH)CO2]2Ca.H2O (VII), which dried 2 hrs. at 100° and 0.01 mm. over P2O5 gave anhydrous VII, m. 215-20° (with slight decomposition), [α]22D 20° (c 0.5, H2O). VII debenzylated catalytically with H and Pd gave D-[HOCH2CH(OH)CO2]2Ca, [α]23D 11.8°. VII (9 g.) in 50 cc. N HCl extracted with four 50-cc. portions Et2O, and the extract dried, treated with 2.0 g. CH2N2 in Et2O, and evaporated after 0.5 hr. in vacuo finally at 50° gave 8.5 g. Me ester (VIII) of PhCH2OCH2CH(OH)CO2H (IX), sirup, [α]D -1.31°, which distilled at 0.1 mm. gave a middle fraction, b0.1 95-100°, d25 1.160, [α]D -1.45. VIII reduced with LiAlH4 gave a benzylglycerol which consumed 1 mole NaIO4/188 g.; the debenzylation of the O-benzylglycerol (X) gave the expected glycerol, isolated as the tribenzoate, m. 74-6°. VIII (8.0 g.) in 40 cc. dry pyridine cooled to 5° and treated dropwise during 10 min. with 10.8 g. Ph2POCl, the mixture allowed to stand overnight at 5-10°, treated with 1 cc. H2O, allowed to stand 0.5 hr., and concentrated in vacuo at 50°, the residue dissolved in 100 cc. CHCl3, and the solution washed with 100-cc. portions H2O, cold N HCl, cold N KHCO3, and again H2O, and evaporated to dryness in vacuo yielded 16.0 g. (95%) 2-diphenylphosphoryl derivative (XI) of VIII, sirup. PdCl2-C (5%) (5 g.) in 100 cc. 95% EtOH shaken with H until the uptake was complete, the catalyst washed acid-free with 95% EtOH by repeated suspension and centrifugation (4-5 washings), the washed catalyst resuspended in 100 cc. absolute EtOH, the suspension treated with 5.0 g. XI, the mixture shaken 10-15 min. with H at room temperature and atmospheric pressure, the catalyst centrifuged, the solution treated with 1 g.

freshly prepared PtO2 along with about 1 g. acid-washed C, the mixture shaken vigorously 1 hr. with H, the catalyst centrifuged off, the alc. solution immediately mixed with 25 cc. N NaOH, the resulting turbid solution evaporated in vacuo at 40° bath temperature, the residual sirup dissolved in 10 cc. H2O, the solution treated with 10 cc. N NaOH, allowed to stand 0.5 hr. at room temperature, mixed with a little Filter-Cel, and filtered through Whatman paper number 50, the vessel rinsed and the filter residue washed with about 10 cc. H2O, the combined aqueous filtrates diluted with about 50 cc. MeOH to turbidity, let stand until the 1st crystals deposited, and then cooled overnight at 5°, the crystalline deposit centrifuged off, washed with absolute Et2O, and dried in air, the product (2.0-2.5 g.) redissolved in 15 cc. H2O, the solution filtered with Filter-Cel (if cloudy) and diluted to turbidty with MeOH and allowed to stand overnight at 5° deposited II.5H2O, needles, which centrifuged off, washed twice with MeOH and then Et2O, and dried in air gave pure II.5H2O, [α]22D 3.6° (c 2, H2O); I, [α]22D 12.9° (c 1.8, N HCl). II.5H2O dried 6 hrs. at 80° and 0.01 mm. lost all the water of hydration but regained the weight loss upon reequilibration in a moist atmospheric II showed [α]21D 13.0° (c 2.4 I, N HCl) (64.4 mg. II in 2 cc. N HCl); the rotation in neutral 25% NH4 molybdate solution was [α]22D 5°. The discrepancy between the rotations of this preparation and the Meyerhof and **Kiessling** preparation (-68°) (loc. cit.) in molybdate is due to a contaminant of about 10% 3-phosphoryl-D-glyceric acid (XII) in the product obtained by M. and K. A sample of I heated 18 hrs. at 125° in a sealed tube with N HCl, the acid solution treated with excess Ba(OAc)2 and NaOH equivalent to the acid, and the mixture filtered gave a filtrate having [α]D 10.9° comparing well with the value of 12° reported for Ba D-glycerate. HCl containing 0.8% II heated in a water bath, 0.5-cc. aliquots taken periodically and added to 0.5 cc. NaOH equivalent to the acid, the mixture treated with 1 cc. 25% NH4 molybdate, and the rotation of the mixture determined in a 1-cm. tube showed that I was stable for at least 2 hrs. in 0.25N HCl at 50°, but at higher temps. migration occurred, and was very rapid in N HCl at 100°; no inorg. phosphate was formed during the reaction. II (about 200 mg.) in 5 cc. N HCl heated 1 hr. at 100°, the hot solution treated with 40% aqueous Ba(OAc)2 until it became turbid, the inner wall rubbed with a glass rod, the mixture allowed to stand 4 hrs. at 5°, and the salt centrifuged, washed twice with 5-cc. portions 50% EtOH, once with absolute EtOH, and dried 1 hr. in vacuo at 80° and 0.01 mm. yielded 150 mg. (90%) Ba salt of XII; 45.2 mg. Ba salt in 2.0 cc. N HCl showed αD -0.17° (1 dm.), or [α]D -14.3° (c 1.19 XII, N HCl); 0.5 cc. of the acid solution, 0.1 cc. N H2SO4, 0.5 cc. N NaOH, and 1.0 cc. 30% aqueous NH4 molybdate centrifuged to remove the BaSO4 gave a clear supernatant showing [α]D -740° (c 0.283 XII), 15% NH4 molybdate). A purified, but not crystalline, enolase incubated with I at pH 7 and 5° in the presence of 3 + 10-4 MgSO4 showed a rapid increase of the ultraviolet absorption of the solution which came to an equilibrium at a value of 2.5 [phosphorylenolpyruvate (XIII)/2 I] calculated from a mol. extinction coefficient of 1.73 + 103 for XIII. When the action of enolase was coupled with that of phosphopyruvate transphosphorylase and lactic dehydrogenase in the presence of adenosine diphosphate and reduced diphosphopyridine nucleotide, a solution containing 3.36 micromoles/cc. of I assayed 317 micromoles/cc. (95%). II (200 mg.), 1.5 cc. H2O, 0.5 cc. 0.01M MgSO4, and 0.2 cc. enolase solution (5 mg. protein/cc.) allowed to stand 1 hr. at room temperature, the mixture treated with 100 mg. AgNO3 in 2 cc. H2O followed by about 2 cc. N HNO3 (dropwise), the mixture centrifuged, the supernatant decanted, treated with 2 cc. 40% aqueous Ba(OAc)2 and allowed to stand in the dark at room temperature overnight, the solution decanted from the crystalline deposit, and the residue washed with four

5-cc. portions 50% EtOH and then twice with absolute EtOH, and dried in vacuo at room temperature over P2O5 yielded 160 mg. (87%) XIII.

L2 ANSWER 29 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI The molybdenum-nitrogen and the tungsten-nitrogen systems
AB cf. following abstrs. New data from x-ray diffraction patterns of nitrides, prepared by heating finely powdered Mo and W in a constant stream of dry NH3 up to 800° for a few hrs., are reported. α, β, and γ phases in the Mo-N system and α and β phases in the W-N system previously reported by Hagg (C.A. 24, 3688) are confirmed. A γ phase in the system W-N, reported by **Kiessling** and Liu (C.A. 45, 7906b) was not confirmed. The previously known simple hexagonal lattice of MoN(δ) exhibits a hexagonal superstructure formed by doubling the axes of the substructure. The new unit cell contains 8 units MoN. In the W-N system a new phase, δ, was found with composition close to the formula WN. It is isomorphous with WC and is less stable than MoN at high temps.

L2 ANSWER 30 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI Borides with higher content of boron
AB The structures of borides of the type XB4, XB5, (XNa)B6, and XB12 are described, X being an element in which the d shell immediately below the valency electrons is empty. The coordination of B atoms by B is 3 or 5. The B radii are of 2 kinds: in the rigid covalent B-B bonds the radius varies little from 0.86 A.; in the B-metal bonds, however, it varies between 0.86 and 1.10 A. Pauling's theory (C.A. 41, 5772i) does not give a satisfactory quant. evaluation of the valencies in these borides; **Kiessling** (C.A. 45, 7906b) reached a similar conclusion in his study of borides of lower B content.

L2 ANSWER 31 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI A new molybdenum carbide
AB Mo and CO produce along with the β-phase (Mo2C) and γ-phase (MoC), a new γ'-phase, which transforms rapidly above 800° in vacuo or in CO to the γ-phase. The last may also be the stable phase at low temperature From the lack of change in the powder photograph during this transformation, and from the lattice spacing, the formula for the new phase appears to be MoC. The metallic lattice is similar to that of W2B5 (cf. **Kiessling**, C.A. 42, 5738d). The carbon positions could not be located. There are 2, 1, and 4 Mo atoms, resp., in the three phases. The lattices may be symbolized by ABAB, AAAA, and AABBAABB, resp. Thus the γ'-phase is intermediate, but there is no indication of stacking disorder. The space group is C 6/mmc with Mo in 4 (f) positions and with z = 1/8. Lattice dimensions are given for all three.

L2 ANSWER 32 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI A new coenzyme of alcoholic fermentation
AB cf. C.A. 37, 2762.8. Fresh yeast contains a factor which enables yeast maceration juice at a very low level of orthophosphate to ferment glucose about 3 times faster than adenosine triphosphate does. A crude preparation of the cofactor was purified about 40-fold by alc. precipitation and ion-exchange chromatography; it has the properties of a nucleotide. The coenzyme acts by stimulating the formation of an unknown phosphate-splitting compound An improvement of **Kiessling**'s method (C.A. 29, 4330.8; 31, 372.8) for preparing pure crystalline phosphopyruvate (Ag Ba salt) is described.

L2 ANSWER 33 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI Studies on hepatic glycolysis
AB Hepatic glycolysis involves phosphorylation mechanisms similar to muscular glycolysis since phosphates and adenosine triphosphate favor formation of lactic acid (I) while fluorides, accompanied by esterification of phosphates, inhibit I. The glycolytic enzyme system depends largely on maintenance of cellular integrity; glycolysis does not occur in hepatic

exts., but requires an insol. enzyme which probably is involved before phosphorylation. Only phosphoglyceric and pyruvic acids can be shown, directly, to be intermediate substrates. The roles of hexose diphosphate and hexoseglycerophosphate follow from their accumulation in the presence of fluorides while the roles of mono- and diphosphoric acid esters follow from their activity in the presence of fluorides and pyruvic acid. Embden's dismutation (E., et al., C.A. 27, 2190) does not occur in hepatic tissue while that of Meyerhoff and **Kiessling** (C.A. 30, 1857.9) is not as important as it is in muscle tissue.

L2 ANSWER 34 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI Phosphorylation with polyphosphoric acids
AB Polyphosphoric acids, HOPO(OH)O[PO(OH)O]nPO(OH)(OH) (I), obtained by thermal dehydration of H3PO4, are analyzed for their degree of polymerization by fractional titration with methyl orange and thymolphthalein as indicators in the presence of neutral CaCl2. I possesses for each P atom one strongly acid OH, and for each terminal P atom one more weakly acid OH. For the phosphorylation with I (n = 0), 2 g. of its Na salt is heated on a water bath with 38.2 cc. absolute EtOH containing the theoretical amount of HCl to liberate I. Intermittent titrations show that the reaction is complete in 1 hr. From the reaction mixture 90% EtOPO3Ca.2H2O is isolated. Titration of a reaction mixture of the Na salt of I (n = 1) and EtOH-HCl, after it has been heated 15 min., indicates the formation of EtOPO3H2 and (EtO)2PO2H in a ratio of 9:1. From the reaction mixture 35% EtOPO3Ba.H3O is isolated. When 20 g. I (n = 3) and 10 g. absolute MeOH are heated 30 hrs., titrations with methyl orange and thymolphthalein give almost identical results, indicating that the formation of (MeO)2PO2H is very small. From the reaction mixture 84% MeOPO3Ba and 1.5% (MeO)4P2O4Ba.5H2O are isolated. I (n = 2) and PhCH2OH give 31% PhCH2OPO3Ba.H2O. Cetyl alc. and I (n = 3) refluxed 2-3 hrs. give C16H33OPO3Ba, from which the free C16H33OPO3H2, needles, m. 69-75°, is isolated by acidification and extraction with ether. Lactic acid (4.8 g.) and 4.5 g. I (n = 3.1) heated 3 hrs. on a water bath give 8.2% HO2CCHMe(OPO3Ba1.5).2H2O (cf. Wagner-Jauregg, C.A. 29, 4330.6). MeCOCO2H (6.18 g.) and 7.3 g. I (n = 2.5) are mixed and kept 16 hrs. at 0°. Neutralization of the mixture with Ba(OH)2, concentration, and addition of EtOH give 35% of a product very soluble in cold H2O, much less soluble in hot H2O, and insol. in EtOH. It decolorizes KMnO4 instantly with formation of H3PO4 and is apparently an enolic pyruvic-phosphoric acid (cf. **Kiessling**, C.A. 31, 372.6). When 2 g. H2NCH2CH2OH and 6.8 g. I (n = 1.7) are heated 1 hr. on a water bath, the cooled mixture neutralized with BaCO3 and with Ba(OH)2 to pH 9.4, 60% crude Ba salts are obtained from which 52% H2NCH2CH2OPO3H2, fine long needles, m. 233-5°, is obtained with H2SO4. Choline and I (n = 2) give 45.5% choline phosphoric acid. Glycol and I readily give glycol phosphoric acid, and glycerol and I, a mixture of α- and β-glycerophosphoric acids. I do not phosphorylate N bases such as PhNH2 or creatine. A comparison of the phosphorylating action of I with that of P2O5 or POCl3 shows that I gives chiefly monoalkoxyphosphoric acids.

L2 ANSWER 35 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI Synthesis of d(-)-3-phosphoglyceric acid and d(+)-2-phosphoglyceric acid
AB cf. C. A. 27, 5764; Meyerhof and **Kiessling**, C. A. 29, 3453.7. On mixing d-glyceric acid with EtPO3, d(-)-3-phosphoglyceric and d(+)-2-phosphoglyceric acids are formed approx. in the ratio of 10:1. The optical activities are resp. [α]18D -13.27° and [α]22D 23.2°.

L2 ANSWER 36 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI Dissimilation of phosphoglyceric acid by Escherichia coli
AB Cell-free exts. obtained by grinding Es. coli with powdered glass contained

enzymes which converted phosphoglyceric acid to phosphopyruvic acid (I). The effect of temperature on the reaction agreed with the results of Meyerhof and **Kiessling** for muscle and yeast (C. A. 29, 3453.7, 8024.8). (-)3-Phosphoglyceric acid and (+)2-phosphoglyceric acids established the same equilibrium in bacteria as in muscle and yeast but differed with regard to the optical specificity reported for lactic acid bacteria by Katagiri and Murakami (C. A. 33, 9358.7). The equilibrium was shown to be truly reversible. Mg or Mn seemed to stimulate the phosphoglyceromutase-enolase equilibrium I transferred phosphate to adenylic acid (II). The phosphate from I was partially transferred to glucose via II when glucose was added; hexosemonophosphate did not replace glucose.

L2 ANSWER 37 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI Diose phosphate. I. Oxidation to phosphoglycolic acid and some properties of this acid
AB Diose phosphate, (HO)2P(:O)OCH2CHO, is oxidized by hypoiodite to phosphoglycolic acid (I), (HO)2P(:O)OCH2CO2H, identified in the form of its hydrated tri-Ba salt, (BaO2P(:O)OCH2CO2)2Ba.4H2O (II). II treated with the theoretical quantity of dilute H2SO4 or HCl gives the acid salt, HOPO2OCH2CO2Ba.H2O, previously described by **Kiessling** (C. A. 29, 2510.2). I is hydrolyzed by phosphatase of sweet almonds and taka-diastase. Hydrolysis by the latter is analogous to that of other phosphoric esters of acid alcs.

L2 ANSWER 38 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI The effect of dinitrophenols on yeast-maceration juice
AB The induction time of the reaction of maceration juice with glucose is reduced by addition of methylene blue (Meyerhof and **Kiessling**, C. A. 28, 2117.3); a similar effect is obtained upon addition of 1,2,5- or 1,2,4-dinitrophenol in 10-3 to 10-5 molar dilution The 1,2,6-compound is inactive. The induction period for levulose, mannose and sucrose is likewise shortened. The dinitrophenols do not affect the fermentation of hexosediphosphate. Higher concns. than 10-3 molar inhibit glucose fermentation because of inhibition of carboxylase.

L2 ANSWER 39 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI Chlorophyll. LXXXVI. Acetylrhodine g7 and several vinylporphyrins
AB cf. C. A. 33, 4264.1. Rhodine g7 tri-Me ester (1 g.), shaken 3.5 hrs. with 50 g. HBr-AcOH, gives 1.4 g. of 2-α-bromomesorhodine g7, which was not purified but immediately hydrolyzed with 20% HCl to 2-α-hydroxymesorhodine g7 (I), C37H42O8N4, separated by extraction from Et2O with 8% HCl and esterified with CH2N2 (tri-Me ester), bluish black, m. 185°. Heating I 10 min. in a high vacuum at 195° gives rhodine g7. I, shaken with finely powdered Na2Cr2O7 in C5H5N for 48 hrs., gives after esterification 2-acetylrhodine g7, C37H40O8N4, bluish black, m. 263°. Methylpheophorbide A(II) and Fe powder in boiling HCO2H(3.5 min.) give a leuco compound, which is added to Et2O and the HCO2H removed with NH4OH; on standing overnight (reoxidation of leuco compound), extraction with 12% HCl and esterification with CH2N2, 200 mg. II (in 50-mg. portions) give 60 mg. vinylpheoporphyrin a5 di-Me ester (III), m. 288-92°; 80% HCO2H at 70-80° gives the same yield (cf. Noack and **Kiessling**, C. A. 23, 3249); III also results in 35-mg. yield from 50 mg. vinylchloroporphyrin e6 tri-Me ester (IV) and 300 mg. Na2CO3 in 30 cc. C5H5N on boiling 2 hrs. III with NH2OH.HCl and AcOK in C5H5N, heated 1.5 hrs. on the water bath, gives an oxime, m. 286°. Warming III with EtMgBr in PrOH or iso-PrOH and C5H5N gives the phyllin and Fe(OAc)2-NaCl in boiling AcOH(5 min.) gives the hemin, which may form a HCl salt, C36H35O6N4FeCl2. The Cu complex of III, C36H34O5N4Cu, needles, m. above 320°. Chlorine e6 tri-Me ester (200 mg.) and Fe in boiling 80% HCO2H give 100 mg. of IV; IV also results from III by treating 50 mg. in C5H5N-MeOH with 5 cc. of 10% MeOH-KOH. The Cu complex of IV, C36H38O6N4Cu, prisms, m. 222°. Catalytic reduction (Pd) of III gives pheoporphyrin a5 (V); reduction with HI in AcOH at 65°

also gives V. Pyropheophorbide a (200 mg.) gives 65 mg. of vinylphylloerythrin, C34H34O3N4, m. 278°; the Et2O solution has a red color with a blue-green fluorescence; the N2CCO2Et derivative forms blue-violet needles. III with cold AcOH-HI gives V and not the oxo derivative 10-Acetoxyvinylpheoporphyrin a5 (VI) with H2SO4 (3 hrs. at 0°), followed by 100% HCO2H at 60°, gives III. VI with AlCl3 in boiling CHCl3 also gives III. VI in C5H5N-EtOH, shaken with 10% MeOH-KOH for 45 min., gives 20% vinylpheoporphyrin a7, m. 274-6°.

L2 ANSWER 40 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI Mechanism of the enzymic breakdown of carbohydrates (formation of lactic acid and alcoholic fermentation)
AB An extensive review, largely of the work in recent years of O. Meyerhof, K. Lohmann and W. **Kiessling**.

L2 ANSWER 41 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI The participation of adenylic acid and cozymase in phosphorylation by displacement and reesterification
AB The rate of fermentation in the system: apozymase, glucose (I), synthetic phosphopyruvic acid (II) (cf. Meyerhoff and **Kiessling**, C. A. 29, 8024.8) is increased by the addition of increasing amts. of adenylic acid (III). E. and A. propose that III acts as phosphate carrier from II to I. In light of previous work (C. A. 29, 6908.9) and of this observation, it is concluded that III acts as a phosphate-transferring catalyst in the enzyme-coenzyme system of yeast fermentation. The presence of III is not necessary for fermentation, however. Cozymase, free from III and inactivated as an oxidation-reduction catalyst, retains its phosphate-transferring activity. This activity is ascribed to a part of the cozymase mol. having the adenylic acid grouping. A reduced substance that cannot be reoxidized by methylene blue or air, but is reoxidized by flavin enzyme, is produced from dehydrogenase and alc. by cozymase. Cozymase prepns. have been separated by chromatographic analysis into cozymase and a "second activator." The latter seems to be identical with Warburg's coenzyme obtained from horse blood.

L2 ANSWER 42 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI Estimation of acidity in barley by titration in stages
AB By titrating barley exts. with alkali using litmus paper and phenolphthalein in turn, it is possible to gain some insight into the character of the acid substances present. The "litmus acidity" (=A) is constituted mainly of free acids and acid salts, while the "phenolphthalein or total acidity" (=B) includes feebly acid and amphoteric substances, such as the lower products of proteolysis. For the extraction of the acidic substances in barley the method of Adler and Luers was employed in preference to that described by Belohoubek (hot water extraction). Five g. of ground barley were thoroughly triturated with 8-10 cc. of 96% alc. and the mixture heated for 20 min. in a bath of 80° to evaporate all the alc. The residue was thoroughly mixed with 100 cc.CHCl3-water and allowed to stand for at least 3 hours with occasional stirring. The mixture was then titrated with 0.1 N alkali using litmus paper and phenolphthalein in turn as indicators. In applying this method to the study of the pre-existing acidity of barley, it was observed that barley not fully matured by storage showed a higher B than A, while for those which had undergone after-ripening B and A were practically alike. This indicates a disappearance of amino acids during the process of after-ripening as was already noted by **Kiessling** and Schjerning. The above results appear to indicate, therefore, that practical identity of A and B, when determined by the method described, is a mark of complete ripeness in a barley and, consequently, of its fitness for malting. It sometimes happened, however, that a barley which, judged by this standard, had not fully ripened, possessed a high germinating capacity. Expts. were made with a view to finding a quant. measure of the enzymic strength of barley in the acidity developed by enzymic processes when the ground barley is digested

with water, e. g., for 15 hrs. at 18-19. It was found that A increased only slightly or not at all during digestion, while the increase in B is considerable. Although further data will be required before definite general conclusions of practical value can be drawn, the expts. appear to indicate that the increase of acidity on digestion is a seasonal character of barley and is in general greater for barleys of high germinating power.

L2 ANSWER 43 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI Estimation of acidity in barley by titration in stages
AB By titrating barley exts. with alkali using litmus paper and phenolphthalein in turn, it is possible to gain some insight into the character of the acid substances present. The "litmus acidity" (=A) is constituted mainly of free acids and acid salts, while the "phenolphthalein or total acidity" (=B) includes feebly acid and amphoteric substances, such as the lower products of proteolysis. For the extraction of the acidic substances in barley the method of Adler and Luers was employed in preference to that described by Belohoubek (hot water extraction). Five g. of ground barley were thoroughly triturated with 8-10 cc. of 96% alc. and the mixture heated for 20 min. in a bath of 80° to evaporate all the alc. The residue was thoroughly mixed with 100 cc.CHCl3-water and allowed to stand for at least 3 hours with occasional stirring. The mixture was then titrated with 0.1 N alkali using litmus paper and phenolphthalein in turn as indicators. In applying this method to the study of the pre-existing acidity of barley, it was observed that barley not fully matured by storage showed a higher B than A, while for those which had undergone after-ripening B and A were practically alike. This indicates a disappearance of amino acids during the process of after-ripening as was already noted by **Kiessling** and Schjerning. The above results appear to indicate, therefore, that practical identity of A and B, when determined by the method described, is a mark of complete ripeness in a barley and, consequently, of its fitness for malting. It sometimes happened, however, that a barley which, judged by this standard, had not fully ripened, possessed a high germinating capacity. Expts. were made with a view to finding a quant. measure of the enzymic strength of barley in the acidity developed by enzymic processes when the ground barley is digested with water, e. g., for 15 hrs. at 18-19. It was found that A increased only slightly or not at all during digestion, while the increase in B is considerable. Although further data will be required before definite general conclusions of practical value can be drawn, the expts. appear to indicate that the increase of acidity on digestion is a seasonal character of barley and is in general greater for barleys of high germinating power.

L2 ANSWER 44 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI Glue Testing by Means of Cambon's Fusiometer
AB **Kiessling**'s method of determining the melting point of glue has several disadvantages, notably the liability of the glue to undergo change during the long heating required to prepare the 33 1/3% solution used, and the practical difficulty of determining the temperature at which melting begins. The authors have tested a method using an apparatus devised by Victor Cambon called a "fusiometer." The apparatus used is indicated in the figure. It consists of the metal cup (a) 22 mm. high, 17 mm. in diameter at the top and 15 mm. at the bottom, and weighing 7 g. The exact dimensions are not of great importance, but the weight should be adjusted to exactly 7 g. The bottom of the cup of iron is 3 mm. thick. Ferrules such as are used on walking canes answer very well. The part (b) consists of a cylinder of reed or wood 45 mm. long and 8 mm. in diameter with a hole bored near the top through which passes an iron or copper wire 160 mm. long. In addition to this apparatus a water-bath, a beaker 15 cm. high and 10 cm. inside diameter, a ring of 5 cm. diameter, a vertical support and a thermometer graduated to 0.1° are required, 2 g. of glue are accurately weighed and placed in a test tube with 8 cc. water. The tube is well corked and allowed to stand overnight at room temperature. The glue is then dissolved by holding the tube in warm

water, not over 60°. By shaking the tube a homogeneous liquid is easily obtained. In the meantime the metal cup is set on a horizontal surface and the stick b suspended vertically in the middle of the cup, so that it is only a short distance above the bottom. The glue solution is poured into the cup and allowed to set to a jelly. This may be hastened by setting the cup in ice water. The beaker is filled 2/3 with water at 15° and set on the water-bath which is at 50°, the fusiometer is hung by the wire in the middle of the beaker with the thermometer near it in the water and the temperature observed at which the metal cup drops. Results obtained with eighteen different samples of glue are given. The best grades of glue show a melting point of above 30.°3 (30-32°5 and inferior grades from 24.5-25.°5).

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=> d his

     (FILE 'HOME' ENTERED AT 16:52:08 ON 18 MAY 2004)

     FILE 'MEDLINE, BIOSIS, EMBASE, SCISEARCH, CAPLUS, WPIDS' ENTERED AT
     16:53:00 ON 18 MAY 2004
                E KIESSLING
L1            54 S E3
L2            44 DUP REM L1 (10 DUPLICATES REMOVED)

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E1             1     AU9NB11/BI
E2             1     AU9SH/BI
E3             0 --> AU=KIESSLING/BI
E4          1865     AUA/BI
E5           148     AUA1/BI
E6             5     AUA2/BI
E7             1     AUA2CL/BI
E8             1     AUA2S/BI
E9            10     AUA3/BI
E10            8     AUA4/BI
E11            1     AUA6/BI
E12            3     AUA6665/BI

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E1             1     KIESSLIN R/AU
E2             1     KIESSLINE B/AU
E3             2 --> KIESSLING/AU
E4           302     KIESSLING A/AU
E5           253     KIESSLING A A/AU
E6             1     KIESSLING A D/AU
E7             2     KIESSLING A G/AU
E8            40     KIESSLING A H/AU
E9             8     KIESSLING A J/AU
E10            4     KIESSLING A K/AU
E11           22     KIESSLING ANDERS/AU
E12            3     KIESSLING ANDERS K/AU

=> e kiessling l/au
E1             1     KIESSLING KLAUS/AU
E2             1     KIESSLING KUNZE M S/AU
E3            43 --> KIESSLING L/AU
E4            43     KIESSLING L A/AU
E5             3     KIESSLING L E/AU
E6           235     KIESSLING L L/AU
E7            74     KIESSLING L S/AU
E8             2     KIESSLING LAESSIG A/AU
E9             5     KIESSLING LAURA/AU
E10          252     KIESSLING LAURA L/AU
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E11           1      KIESSLING LAURA LEE/AU
E12           2      KIESSLING LEIF/AU

=> s e6 39 e10 e11

EXCEEDS MAXIMUM FIELD LENGTH, WILL BE SEARCHED AS 'KIESSLING L L"/AU 39 "KIESSLING
LAURA L"/AU "KIESSLI/AU'

EXCEEDS MAXIMUM FIELD LENGTH, WILL BE SEARCHED AS 'KIESSLING L L"/AU 39 "KIESSLING
LAURA L"/AU "KIESSLI/AU'

EXCEEDS MAXIMUM FIELD LENGTH, WILL BE SEARCHED AS 'KIESSLING L L"/AU 39 "KIESSLING
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EXCEEDS MAXIMUM FIELD LENGTH, WILL BE SEARCHED AS 'KIESSLING L L"/AU 39 "KIESSLING
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EXCEEDS MAXIMUM FIELD LENGTH, WILL BE SEARCHED AS 'KIESSLING L L"/AU 39 "KIESSLING
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EXCEEDS MAXIMUM FIELD LENGTH, WILL BE SEARCHED AS 'KIESSLING L L"/AU 39 "KIESSLING
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L3            0 "KIESSLING L L"/AU 39 "KIESSLING LAURA L"/AU "KIESSLING LAURA
                LEE"/AU

=> s e6 or  e9 or e10 or e11
L4          493 "KIESSLING L L"/AU OR "KIESSLING LAURA"/AU OR "KIESSLING LAURA
                L"/AU OR "KIESSLING LAURA LEE"/AU

=> d his

     (FILE 'HOME' ENTERED AT 16:52:08 ON 18 MAY 2004)

     FILE 'MEDLINE, BIOSIS, EMBASE, SCISEARCH, CAPLUS, WPIDS' ENTERED AT
     16:53:00 ON 18 MAY 2004
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L1           54 S E3
L2           44 DUP REM L1 (10 DUPLICATES REMOVED)
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                E KIESSLING/AU
                E KIESSLING L/AU
L3            0 S E6 39 E10 E11
L4          493 S E6 OR  E9 OR E10 OR E11

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5          284 DUP REM L4 (209 DUPLICATES REMOVED)

=> s l5 and ligand
L6           53 L5 AND LIGAND

=> d ti 1-53

L6   ANSWER 1 OF 53     MEDLINE on STN
TI   Trophoblast L-selectin-mediated adhesion at the maternal-fetal interface.

L6   ANSWER 2 OF 53     MEDLINE on STN
TI   Influencing receptor-ligand binding mechanisms with multivalent
     ligand architecture.

L6   ANSWER 3 OF 53     MEDLINE on STN
TI   Synthesis of a multivalent display of a CD22-binding trisaccharide.
```

L6 ANSWER 4 OF 53 MEDLINE on STN
TI Selective immobilization of multivalent ligands for surface plasmon resonance and fluorescence microscopy.

L6 ANSWER 5 OF 53 MEDLINE on STN
TI Control of multivalent interactions by binding epitope density.

L6 ANSWER 6 OF 53 MEDLINE on STN
TI Cell aggregation by scaffolded receptor clusters.

L6 ANSWER 7 OF 53 MEDLINE on STN
TI Inter-receptor communication through arrays of bacterial chemoreceptors.

L6 ANSWER 8 OF 53 MEDLINE on STN
TI Synthetic multivalent ligands in the exploration of cell-surface interactions.

L6 ANSWER 9 OF 53 MEDLINE on STN
TI Tuning chemotactic responses with synthetic multivalent ligands.

L6 ANSWER 10 OF 53 MEDLINE on STN
TI Synthesis of end-labeled multivalent ligands for exploring cell-surface-receptor-**ligand** interactions.

L6 ANSWER 11 OF 53 MEDLINE on STN
TI Inhibition of L-selectin-mediated leukocyte rolling by synthetic glycoprotein mimics.

L6 ANSWER 12 OF 53 MEDLINE on STN
TI L-selectin-carbohydrate interactions: relevant modifications of the Lewis x trisaccharide.

L6 ANSWER 13 OF 53 MEDLINE on STN
TI Specificity of C-glycoside complexation by mannose/glucose specific lectins.

L6 ANSWER 14 OF 53 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
TI Using multivalent ligands to study B cell activation.

L6 ANSWER 15 OF 53 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
TI The chemistry and biology of multivalent saccharide displays.

L6 ANSWER 16 OF 53 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
TI Assembling systems of interacting proteins with synthetic ligands.

L6 ANSWER 17 OF 53 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
TI Synthesis of sulfated Lewis x polymers and their affinity for L-selectin.

L6 ANSWER 18 OF 53 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
TI Tuning cellular responses with synthetic, multivalent ligands.

L6 ANSWER 19 OF 53 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
TI Mechanistic origins of the valency effect: Multivalent **ligand** binding studied by surface plasmon resonance and isothermal titration calorimetry.

L6 ANSWER 20 OF 53 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
TI Total synthesis of polymeric 6-sulfo sialyl Lewis x as a multivalent **ligand** for L-selectin.

L6 ANSWER 21 OF 53 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
TI Modulating cell surface protein function with defined, polymeric ligands.

L6 ANSWER 22 OF 53 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
TI Controlling cell surface molecule display with **ligand**-activated proteolysis.

L6 ANSWER 23 OF 53 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
TI Multivalent saccharide ligands.

L6 ANSWER 24 OF 53 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
TI Designing modulators of cell-cell interactions: Exploring monovalent and multivalent carbohydrate ligands.

L6 ANSWER 25 OF 53 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI Synergistic formation of soluble lecfin clusters by a templated multivalent saccharide **ligand** [6].

L6 ANSWER 26 OF 53 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI Scope of multivalent **ligand** function: Lactose-bearing neoglycopolymers by ring-opening metathesis polymerization.

L6 ANSWER 27 OF 53 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI A general synthetic route to defined, biologically active multivalent arrays.

L6 ANSWER 28 OF 53 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI Probing low affinity and multivalent interactions with surface plasmon resonance: Ligands for concanavalin A.

L6 ANSWER 29 OF 53 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI Synthetic ligands point to cell surface strategies [8].

L6 ANSWER 30 OF 53 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI Varying the size of multivalent ligands: The dependence of concanavalin A binding on neoglycopolymer length.

L6 ANSWER 31 OF 53 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
TI Mechanistic origins of the valency effect: Multivalent **ligand** binding studied by surface plasmon resonance and isothermal titration calorimetry.

L6 ANSWER 32 OF 53 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
TI Total synthesis of polymeric 6-sulfo sialyl Lewis X as a multivalent **ligand** for L-selectin.

L6 ANSWER 33 OF 53 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
TI Visualization of single multivalent receptor-**ligand** complexes by transmission electron microscopy

L6 ANSWER 34 OF 53 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
TI Principles for multivalent **ligand** design

L6 ANSWER 35 OF 53 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
TI Controlling cell surface molecule display with **ligand**-activated proteolysis.

L6 ANSWER 36 OF 53 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
TI SYNTHESIS OF SIALYL LEWIS-X AS A **LIGAND** FOR STUDIES WITH E-SELECTIN

L6 ANSWER 37 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
TI Synthetic multivalent carbohydrate ligands as effectors or inhibitors of biological processes

L6 ANSWER 38 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
TI Synthesis and binding mechanisms of polymeric multivalent ligands

L6 ANSWER 39 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
TI Design and fabrication of surfaces for the combinatorial exploration of cell adherence and differentiation

L6 ANSWER 40 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
TI Assembling systems of interacting proteins with synthetic ligands

L6 ANSWER 41 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
TI Chemical approaches to eliciting and inhibiting immune responses

L6 ANSWER 42 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
TI Methods and reagents for regulation of cellular responses in biological systems

L6 ANSWER 43 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
TI Mechanistic origins of the valency effect: Multivalent **ligand** binding studied by surface plasmon resonance and isothermal titration calorimetry

L6 ANSWER 44 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
TI Total synthesis of polymeric 6-sulfo sialyl Lewis x as a multivalent **ligand** for L-selectin.

L6 ANSWER 45 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
TI Exploring receptor interactions with materials generated via metathesis reactions.

L6 ANSWER 46 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
TI Tuning cellular responses with synthetic, multivalent ligands

L6 ANSWER 47 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
TI The molecular recognition of saccharides and glycoprotein-inspired materials

L6 ANSWER 48 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
TI Modulating cell surface protein function with defined, polymeric ligands.

L6 ANSWER 49 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
TI Controlling cell surface molecule display with **ligand**-activated proteolysis.

L6 ANSWER 50 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
TI Synthesis of lactose polymers for the galectins by ring-opening metathesis polymerization.

L6 ANSWER 51 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
TI Multivalent saccharide ligands

L6 ANSWER 52 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
TI Structure-function studies on neoglycopolymers produced by aqueous ring-opening metathesis polymerization.

L6 ANSWER 53 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
TI Designing modulators of cell-cell interactions: Exploring monovalent and multivalent carbohydrate ligands.

=> d 16 ibib abs 1-53

L6 ANSWER 1 OF 53 MEDLINE on STN
ACCESSION NUMBER: 2003025511 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12532021
TITLE: Trophoblast L-selectin-mediated adhesion at the maternal-fetal interface.
COMMENT: Comment in: Science. 2003 Jan 17;299(5605):355-6. PubMed ID: 12532005
AUTHOR: Genbacev Olga D; Prakobphol Akraporn; Foulk Russell A; Krtolica Ana R; Ilic Dusko; Singer Mark S; Yang Zhi-Qiang; **Kiessling Laura L**; Rosen Steven D; Fisher Susan J
CORPORATE SOURCE: Departments of Stomatology, Anatomy, and Pharmaceutical Chemistry, University of California, San Francisco, CA 94143, USA.
CONTRACT NUMBER: DE 07244 (NIDCR)
HL 64597 (NHLBI)
R37GM23547 (NIGMS)
U01 HD 42283 (NICHD)
SOURCE: Science, (2003 Jan 17) 299 (5605) 405-8.
Journal code: 0404511. ISSN: 1095-9203.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 20030118
Last Updated on STN: 20030206
Entered Medline: 20030205

AB Trophoblast adhesion to the uterine wall is the requisite first step of implantation and, subsequently, placentation. At the maternal-fetal interface, we investigated the expression of selectin adhesion systems that enable leukocyte capture from the bloodstream. On the maternal side, human uterine epithelial cells up-regulated selectin oligosaccharide-based ligands during the window of receptivity. On the fetal side, human trophoblasts expressed L-selectin. This **ligand**-receptor system was functional, because beads coated with the selectin **ligand** 6-sulfo sLe(x) bound to trophoblasts, and trophoblasts bound to **ligand**-expressing uterine luminal epithelium in tissue sections. These results suggest that trophoblast L-selectin mediates interactions with the uterus and that this adhesion mechanism may be critical to establishing human pregnancy.

L6 ANSWER 2 OF 53 MEDLINE on STN
ACCESSION NUMBER: 2002713567 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12475334
TITLE: Influencing receptor-**ligand** binding mechanisms with multivalent **ligand** architecture.
AUTHOR: Gestwicki Jason E; Cairo Christopher W; Strong Laura E; Oetjen Karolyn A; **Kiessling Laura L**
CORPORATE SOURCE: Departments of Biochemistry and Chemistry, University of Wisconsin-Madison, Madison, WI 53706, USA.
CONTRACT NUMBER: GM 08349 (NIGMS)
GM 18750 (NIGMS)
GM 49975 (NIGMS)
SOURCE: Journal of the American Chemical Society, (2002 Dec 18) 124 (50) 14922-33.
Journal code: 7503056. ISSN: 0002-7863.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20021217
Last Updated on STN: 20030308
Entered Medline: 20030307

AB Multivalent ligands can function as inhibitors or effectors of biological processes. Potent inhibitory activity can arise from the high functional affinities of multivalent **ligand**-receptor interactions. Effector functions, however, are influenced not only by apparent affinities but also by alternate factors, including the ability of a **ligand** to cluster receptors. Little is known about the molecular features of a multivalent **ligand** that determine whether it will function as an inhibitor or effector. We envisioned that, by altering multivalent **ligand** architecture, ligands with preferences for different binding mechanisms would be generated. To this end, a series of 28 ligands possessing structural diversity was synthesized. This series provides the means to explore the effects of **ligand** architecture on the inhibition and clustering of a model protein, the lectin concanavalin A (Con A). The structural parameters that were varied include scaffold shape, size, valency, and density of binding elements. We found that ligands with certain architectures are effective inhibitors, but others mediate receptor clustering. Specifically, high molecular weight, polydisperse polyvalent ligands are effective inhibitors of Con A binding, whereas linear oligomeric ligands generated by the ring-opening metathesis polymerization have structural properties that favor clustering. The shape of a multivalent **ligand** also influences specific aspects of receptor clustering. These include the rate at which the receptor is clustered, the number of receptors in the clusters, and the average interreceptor distance. Our results indicate that the architecture of a multivalent **ligand** is a key parameter in determining its activity as an inhibitor or effector. Diversity-oriented syntheses of multivalent ligands coupled with effective assays that can be used to compare the contributions of different binding parameters may afford ligands that function by specific mechanisms.

L6 ANSWER 3 OF 53 MEDLINE on STN
ACCESSION NUMBER: 2002663545 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12423961
TITLE: Synthesis of a multivalent display of a CD22-binding trisaccharide.
AUTHOR: Yang Zhi-Qiang; Puffer Erik B; Pontrello Jason K; **Kiessling Laura L**
CORPORATE SOURCE: Department of Chemistry, University of Wisconsin-Madison, Madison, WI 53706, USA.
CONTRACT NUMBER: GM49975 (NIGMS)
RR08389 (NCRR)
SOURCE: Carbohydrate research, (2002 Oct 8) 337 (18) 1605-13. Journal code: 0043535. ISSN: 0008-6215.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 20021109
Last Updated on STN: 20030423
Entered Medline: 20030422

AB Multivalent interactions have been implicated in the binding of B-cell surface glycoprotein CD22 to its physiological ligands. Because CD22 can influence B-cell antigen receptor (BCR) signaling, multivalent ligands that cluster CD22 may influence B-cell responses. Here, we report an efficient synthesis of a fluorophore-labeled multivalent display of a CD22-binding trisaccharide, Neu5Acalpha2,6Galbeta1,4Glc, using the ring-opening metathesis polymerization (ROMP). Our synthetic strategy

involves the modification of an N-hydroxysuccinimide (NHS) ester-substituted polymer generated by ROMP with the aminopropyl glycoside of the trisaccharide. The conjugation efficiency for the coupling is high; when 0.3 equiv of the trisaccharide derivative were used relative to NHS ester groups, the mole fraction (chi) of trisaccharide **ligand** incorporated onto the backbone was 0.3. A fluorescein-labeled version of the multivalent **ligand** binds to cells expressing CD22.

L6 ANSWER 4 OF 53 MEDLINE on STN
ACCESSION NUMBER: 2002312599 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12054443
TITLE: Selective immobilization of multivalent ligands for surface plasmon resonance and fluorescence microscopy.
AUTHOR: Gestwicki Jason E; Cairo Christopher W; Mann David A; Owen Robert M; **Kiessling Laura L**
CORPORATE SOURCE: Department of Chemistry, University of Wisconsin-Madison, Madison, Wisconsin 53706, USA.
CONTRACT NUMBER: GM 08349 (NIGMS)
GM 55984 (NIGMS)
SOURCE: Analytical biochemistry, (2002 Jun 15) 305 (2) 149-55. Journal code: 0370535. ISSN: 0003-2697.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20020611
Last Updated on STN: 20021218
Entered Medline: 20021217

AB Cell surface multivalent ligands, such as proteoglycans and mucins, are often tethered by a single attachment point. In vitro, however, it is difficult to immobilize multivalent ligands at single sites due to their heterogeneity. Moreover, multivalent ligands often lack a single group with reactivity orthogonal to other functionality in the **ligand**. Biophysical analyses of multivalent **ligand**-receptor interactions would benefit from the availability of strategies for uniform immobilization of multivalent ligands. To this end, we report the design and synthesis of a multivalent **ligand** that has a single terminal orthogonal functional group and we demonstrate that this material can be selectively immobilized onto a surface suitable for surface plasmon resonance (SPR) experiments. The polymeric **ligand** we generated displays multiple copies of 3,6-disulfogalactose, and it can bind to the cell adhesion molecules P- and L-selectin. Using SPR measurements, we found that surfaces displaying our multivalent ligands bind specifically to P- and L-selectin. The affinities of P- and L-selectin for surfaces displaying the multivalent **ligand** are five- to sixfold better than the affinities for a surface modified with the corresponding monovalent **ligand**. In addition to binding soluble proteins, surfaces bearing immobilized polymers bound to cells displaying L-selectin. Cell binding was confirmed by visualizing adherent cells by fluorescence microscopy. Together, our results indicate that synthetic surfaces can be created by selective immobilization of multivalent ligands and that these surfaces are capable of binding soluble and cell-surface-associated receptors with high affinity.

L6 ANSWER 5 OF 53 MEDLINE on STN
ACCESSION NUMBER: 2002153140 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11853434
TITLE: Control of multivalent interactions by binding epitope density.
AUTHOR: Cairo Christopher W; Gestwicki Jason E; Kanai Motomu; **Kiessling Laura L**

CORPORATE SOURCE: Department of Chemistry, University of Wisconsin-Madison, Madison, Wisconsin 53706, USA.
CONTRACT NUMBER: GM08349 (NIGMS)
GM55984 (NIGMS)
SOURCE: Journal of the American Chemical Society, (2002 Feb 27) 124 (8) 1615-9.
Journal code: 7503056. ISSN: 0002-7863.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020312
Last Updated on STN: 20020511
Entered Medline: 20020510

AB Receptor clustering by multivalent ligands can activate signaling pathways. In principle, multivalent **ligand** features can control clustering and the downstream signals that result, but the influence of **ligand** structure on these processes is incompletely understood. Using a series of synthetic polymers that vary systematically, we studied the influence of multivalent **ligand** binding epitope density on the clustering of a model receptor, concanavalin A (Con A). We analyze three aspects of receptor clustering: the stoichiometry of the complex, rate of cluster formation, and receptor proximity. Our experiments reveal that the density of binding sites on a multivalent **ligand** strongly influences each of these parameters. In general, high binding epitope density results in greater numbers of receptors bound per polymer, faster rates of clustering, and reduced inter-receptor distances. Ligands with low binding epitope density, however, are the most efficient on a binding epitope basis. Our results provide insight into the design of ligands for controlling receptor-receptor interactions and can be used to illuminate mechanisms by which natural multivalent displays function.

L6 ANSWER 6 OF 53 MEDLINE on STN
ACCESSION NUMBER: 2002146305 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11880031
TITLE: Cell aggregation by scaffolded receptor clusters.
AUTHOR: Gestwicki Jason E; Strong Laura E; Cairo Christopher W; Boehm Frederick J; **Kiessling Laura L**
CORPORATE SOURCE: Department of Biochemistry, University of Wisconsin-Madison, Madison, WI 53706, USA.
CONTRACT NUMBER: GM 08349 (NIGMS)
GM 18750 (NIGMS)
GM 55984 (NIGMS)
SOURCE: Chemistry & biology, (2002 Feb) 9 (2) 163-9.
Journal code: 9500160. ISSN: 1074-5521.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 20020307
Last Updated on STN: 20020702
Entered Medline: 20020701

AB The aggregation of cells by lectins or antibodies is important for biotechnological and therapeutic applications. One strategy to augment the avidity and aggregating properties of these mediators is to maximize the number of their **ligand** binding sites. The valency of lectins and antibodies, however, is limited by their quaternary structures. To overcome this limitation, we explored the use of polymers generated by ring-opening metathesis polymerization (ROMP) as scaffolds to noncovalently assemble multiple copies of a lectin, the tetravalent protein concanavalin A (Con A). We demonstrate that complexes between Con

A and multivalent scaffolds aggregate cells of a T cell leukemia line (Jurkat) more effectively than Con A alone. We anticipate that synthetic scaffolds will offer a new means of facilitating processes that rely on cell aggregation, such as pathogen clearance and immune recognition.

L6 ANSWER 7 OF 53 MEDLINE on STN
ACCESSION NUMBER: 2002054238 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11780121
TITLE: Inter-receptor communication through arrays of bacterial chemoreceptors.
AUTHOR: Gestwicki Jason E; **Kiessling Laura L**
CORPORATE SOURCE: Department of Chemistry, University of Wisconsin-Madison, 53706, USA.
SOURCE: Nature, (2002 Jan 3) 415 (6867) 81-4.
Journal code: 0410462. ISSN: 0028-0836.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20020125
Last Updated on STN: 20020216
Entered Medline: 20020129

AB The sensing mechanisms of chemotactic bacteria allow them to respond sensitively to stimuli. Escherichia coli, for example, respond to changes in chemoattractant concentration of less than 10% over a range spanning six orders of magnitude. Sensitivity over this range depends on a nonlinear relationship between **ligand** concentration and output response. At low **ligand** concentrations, substantial amplification of the chemotactic signal is required; however, the mechanism responsible for this amplification remains unclear. Here we demonstrate that inter-receptor communication within a lattice acts to amplify and integrate sensory information. Synthetic multivalent ligands that interact through the low-abundance, galactose-sensing receptor Trg stabilize large clusters of chemoreceptors and markedly enhance signal output from these enforced clusters. On treatment with multivalent ligands, the response to the attractant serine is amplified by at least 100-fold. This amplification requires a full complement of chemoreceptors; deletion of the aspartate (Tar) or dipeptide (Tap) receptors diminishes the amplification of the serine response. These results demonstrate that the entire array is involved in sensing. This mode of information exchange has general implications for the processing of signals by cellular receptors.

L6 ANSWER 8 OF 53 MEDLINE on STN
ACCESSION NUMBER: 2001110631 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11102876
TITLE: Synthetic multivalent ligands in the exploration of cell-surface interactions.
AUTHOR: **Kiessling L L**; Gestwicki J E; Strong L E
CORPORATE SOURCE: Departments of Chemistry and Biochemistry, University of Wisconsin-Madison, Madison, WI 53706, USA..
kiessling@chem.wisc.edu
CONTRACT NUMBER: GM55984 (NIGMS)
GM8750 (NIGMS)
T32GM08349 (NIGMS)
SOURCE: Current opinion in chemical biology, (2000 Dec) 4 (6) 696-703. Ref: 63
Journal code: 9811312. ISSN: 1367-5931.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010202

AB Processes such as cell-cell recognition and the initiation of signal transduction often depend on the formation of multiple receptor-**ligand** complexes at the cell surface. Synthetic multivalent ligands are unique probes of these complex cell-surface-binding events. Multivalent ligands can be used as inhibitors of receptor-**ligand** interactions or as activators of signal transduction pathways. Emerging from these complementary applications is insight into how cells exploit multivalent interactions to bind with increased avidity and specificity and how cell-surface receptor organization influences signaling and the cellular responses that result.

L6 ANSWER 9 OF 53 MEDLINE on STN
ACCESSION NUMBER: 2000501517 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11048949
TITLE: Tuning chemotactic responses with synthetic multivalent ligands.
AUTHOR: Gestwicki J E; Strong L E; **Kiessling L L**
CORPORATE SOURCE: Department of Chemistry, University of Wisconsin-Madison, 53706, USA.
CONTRACT NUMBER: GM 18750 (NIGMS)
GM 55984 (NIGMS)
T32GM08349 (NIGMS)
SOURCE: Chemistry & biology, (2000 Aug) 7 (8) 583-91.
Journal code: 9500160. ISSN: 1074-5521.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010202

AB BACKGROUND: Multivalent ligands have been used previously to investigate the role of **ligand** valency and receptor clustering in eliciting biological responses. Studies of multivalent **ligand** function, however, typically have employed divalent ligands or ligands of undefined valency. How cells respond to multivalent ligands of distinct valencies, which can cluster a signaling receptor to different extents, has never been examined. The chemoreceptors, which mediate chemotactic responses in bacteria, are localized, and clustering has been proposed to play a role in their function. Using multivalent ligands directed at the chemoreceptors, we hypothesized that we could exploit **ligand** valency to control receptor occupation and clustering and, ultimately, the cellular response. RESULTS: To investigate the effects of **ligand** valency on the bacterial chemotactic response, we generated a series of linear multivalent arrays with distinct valencies by ring-opening metathesis polymerization. We report that these synthetic ligands elicit bacterial chemotaxis in both Escherichia coli and Bacillus subtilis. The chemotactic response depended on the valency of the **ligand**; the response of the bacteria can be altered by varying chemoattractant **ligand** valency. Significantly, these differences in chemotactic responses were related to the ability of the multivalent ligands to cluster chemoreceptors at the plasma membrane. CONCLUSIONS: Our results demonstrate that **ligand** valency can be used to tune the chemotactic responses of bacteria. This mode of regulation may arise from changes in receptor occupation or changes in receptor clustering or both. Our data implicate changes in receptor clustering as one important

mechanism for altering cellular responses. Given the diverse events modulated by changes in the spatial proximity of cell surface receptors, our results suggest a general strategy for tuning biological responses.

L6 ANSWER 10 OF 53 MEDLINE on STN
ACCESSION NUMBER: 2000130934 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10662681
TITLE: Synthesis of end-labeled multivalent ligands for exploring cell-surface-receptor-**ligand** interactions.
AUTHOR: Gordon E J; Gestwicki J E; Strong L E; **Kiessling L L**
CORPORATE SOURCE: Departments of Chemistry and Biochemistry, University of Wisconsin-Madison, Madison, WI 53706, USA.
CONTRACT NUMBER: GM18750 (NIGMS)
GM55984 (NIGMS)
T32GM08349 (NIGMS)
SOURCE: Chemistry & biology, (2000 Jan) 7 (1) 9-16.
Journal code: 9500160. ISSN: 1074-5521.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000327
Last Updated on STN: 20000327
Entered Medline: 20000313

AB BACKGROUND: Ring-opening metathesis polymerization (ROMP) is a powerful synthetic method for generating unique materials. The functional group tolerance of ruthenium ROMP initiators allows the synthesis of a wide range of biologically active polymers. We generated multivalent ligands that inhibit cell surface L-selectin, a protein that mediates lymphocyte homing and leukocyte recruitment in inflammation. We hypothesized that these ligands function through specific, multivalent binding to L-selection. To examine this and to develop a general method for synthesizing multivalent materials with end-labels, we investigated functionalized enol ethers as capping agents in ruthenium-initiated ROMP. RESULTS: We synthesized a bifunctional molecule that introduces a unique end group by terminating ruthenium-initiated ROMP reactions. This agent contains an enol ether at one end and a masked carboxylic acid at the other. We conjugated a fluorescein derivative to an end-capped neoglycopolymer that had previously been shown to inhibit L-selection function. We used fluorescence microscopy to visualize neoglycopolymer binding to cells displaying L-selectin. Our results suggest that the neoglycopolymers bind specifically to cell surface L-selectin through multivalent interactions. CONCLUSIONS: Ruthenium-initiated ROMP can be used to generate biologically active, multivalent ligands terminated with a latent functional group. The functionalized polymers can be labeled with a variety of molecular tags, including fluorescent molecules, biotin, lipids or antibodies. The ability to conjugate reporter groups to ROMP polymers using this strategy has broad applications in the material and biological sciences.

L6 ANSWER 11 OF 53 MEDLINE on STN
ACCESSION NUMBER: 1999150301 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10026133
TITLE: Inhibition of L-selectin-mediated leukocyte rolling by synthetic glycoprotein mimics.
AUTHOR: Sanders W J; Gordon E J; Dwir O; Beck P J; Alon R; **Kiessling L L**
CORPORATE SOURCE: Departments of Chemistry and Biochemistry, University of Wisconsin-Madison, Madison, Wisconsin 53706, USA.
SOURCE: Journal of biological chemistry, (1999 Feb 26) 274 (9) 5271-8.

Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990326
Last Updated on STN: 19990326
Entered Medline: 19990318

AB Synthetic carbohydrate and glycoprotein mimics displaying sulfated saccharide residues have been assayed for their L-selectin inhibitory properties under static and flow conditions. Polymers displaying the L-selectin recognition epitopes 3',6-disulfo Lewis x(Glc) (3-O-SO3-Galbeta1alpha4(Fucalpha1alpha3)-6-O-SO3-Glcbeta+ ++-OR) and 3',6'-disulfo Lewis x(Glc) (3, 6-di-O-SO3-Galbeta1alpha4(Fucalpha1alpha3)Glcbeta-OR) both inhibit L-selectin binding to heparin under static, cell-free binding conditions with similar efficacies. Under conditions of shear flow, however, only the polymer displaying 3',6-disulfo Lewis x(Glc) inhibits the rolling of L-selectin-transfected cells on the glycoprotein **ligand** GlyCAM-1. Although it has been shown to more effective than sialyl Lewis x at blocking the L-selectin-GlyCAM-1 interaction in static binding studies, the corresponding monomer had no effect in the dynamic assay. These data indicate that multivalent ligands are far more effective inhibitors of L-selectin-mediated rolling than their monovalent counterparts and that the inhibitory activities are dependent on the specific sulfation pattern of the recognition epitope. Importantly, our results indicate the L-selectin specificity for one **ligand** over another found in static, cell-free binding assays is not necessarily retained under the conditions of shear flow. The results suggest that monovalent or polyvalent carbohydrate or glycoprotein mimetics that inhibit selectin binding in static assays may not block the more physiologically relevant process of selectin-mediated rolling.

L6 ANSWER 12 OF 53 MEDLINE on STN
ACCESSION NUMBER: 97098108 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8942649
TITLE: L-selectin-carbohydrate interactions: relevant modifications of the Lewis x trisaccharide.
AUTHOR: Sanders W J; Katsumoto T R; Bertozzi C R; Rosen S D; **Kiessling L L**
CORPORATE SOURCE: Department of Chemistry, University of Wisconsin, Madison 53706, USA.
CONTRACT NUMBER: GM23547 (NIGMS)
GM49975 (NIGMS)
NS32254 (NINDS)
+
SOURCE: Biochemistry, (1996 Nov 26) 35 (47) 14862-7.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19970102

AB Protein-carbohydrate interactions are known to mediate cell-cell recognition and adhesion events. Specifically, three carbohydrate binding proteins termed selectins (E-, P-, and L-selectin) have been shown to be essential for leukocyte rolling along the vascular endothelium, the first step in the recruitment of leukocytes from the blood into inflammatory sites or into secondary lymphoid organs. Although this phenomenon is well-established, little is known about the molecular-level interactions

on which it depends. All three selectins recognize sulfated and sialylated derivatives of the Lewis x [Le(x):Gal beta 1-->4(Fuc alpha 1-->3)GlcNAc] and Lewis a [Le(a): Gal beta 1-->3(Fuc alpha 1-->4)GlcNAc] trisaccharide cores with affinities in the millimolar range, and it is believed that variants of these structures are the carbohydrate determinants of selectin recognition. Recently it was shown that the mucin GlyCAM-1, a secreted physiological **ligand** for L-selectin, is capped with sulfated derivatives of sialyl Lewis x [sLe(x): Sia alpha 2-->3Gal beta 1-->4(Fuc alpha 1-->3)GlcNAc] and that sulfation is required for the high-affinity interaction between GlyCAM-1 and L-selectin. To elucidate the important sites of sulfation on Le(x) with respect to L-selectin recognition, we have synthesized six sulfated Le(x) analogs and determined their abilities to block binding of a recombinant L-selectin-Ig chimera to immobilized GlyCAM-1. Our results suggest that 6-sulfo sLe(x) binds to L-selectin with higher affinity than does sLe(x) or 6'-sulfo sLe(x) and that sulfation of sLe(x) capping groups on GlyCAM-1 at the 6-position is important for L-selectin recognition.

L6 ANSWER 13 OF 53 MEDLINE on STN
ACCESSION NUMBER: 96241619 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8639514
TITLE: Specificity of C-glycoside complexation by mannose/glucose specific lectins.
AUTHOR: Weatherman R V; Mortell K H; Chervenak M; **Kiessling L L**; Toone E J
CORPORATE SOURCE: Department of Chemistry, Duke University, Durham, North Carolina 27708-0346 USA.
CONTRACT NUMBER: GM 08349 (NIGMS)
GM 48653 (NIGMS)
GM 49975 (NIGMS)
+
SOURCE: Biochemistry, (1996 Mar 19) 35 (11) 3619-24.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 19960726
Last Updated on STN: 19960726
Entered Medline: 19960715

AB The binding of the mannose/glucose specific lectins from Canavalia ensiformis (concanavalin A) and Dioclea grandiflora to a series of C-glucosides were studied by titration microcalorimetry and fluorescence anisotropy titration. These closely related lectins share a specificity for the trimannoside methyl 3,6-di-O-(alpha-D-mannopyranosyl)-alpha-D-mannopyranoside, and are a useful model system for addressing the feasibility of differentiating between lectins with overlapping carbohydrate specificities. The ligands were designed to address two issues: (1) how the recognition properties of non-hydrolyzable C-glycoside analogues compare with those of the corresponding O-glycosides and (2) the effect of presentation of more than one saccharide recognition epitope on both affinity and specificity. Both lectins bind the C-glycosides with affinities comparable to those of the O-glycoside analogues; however, the ability of both lectins to differentiate between gluco and manno diastereomers was diminished in the C-glycoside series. Bivalent norbornyl C-glycoside esters were bound by the lectin from Canavalia but only weakly by the lectin from Dioclea. In addition to binding the bivalent ligands, concanavalin A discriminated between C-2 epimers, with the manno configuration binding more tightly than the gluco. The stoichiometry of binding of the bivalent ligands to both di- and tetrameric lectin was two binding sites per **ligand**, rather than the expected 1:1 stoichiometry. Together, these results suggest that

concanavalin A may possess more than one class of carbohydrate binding sites and that these additional sites show stereochemical discrimination similar to that of the previously identified monosaccharide binding site. The implications of these findings for possible in vivo roles of plant lectins and for the use of concanavalin A as a research tool are discussed.

L6 ANSWER 14 OF 53 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:535521 BIOSIS
DOCUMENT NUMBER: PREV200300536725
TITLE: Using multivalent ligands to study B cell activation.
AUTHOR(S): Hollenbeck, Jessica J. [Reprint Author]; Puffer, Erik B. [Reprint Author]; Pontrello, Jason K.; **Kiessling, Laura L.**
CORPORATE SOURCE: Department of Biochemistry, University of Wisconsin - Madison, 433 Babcock Dr, Madison, WI, 53706, USA jhollenbeck@biochem.wisc.edu
SOURCE: Abstracts of Papers American Chemical Society, (2003) Vol. 226, No. 1-2, pp. BIOL 39. print.
Meeting Info.: 226th ACS (American Chemical Society) National Meeting. New York, NY, USA. September 07-11, 2003. American Chemical Society.
ISSN: 0065-7727 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Nov 2003
Last Updated on STN: 12 Nov 2003

L6 ANSWER 15 OF 53 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:101280 BIOSIS
DOCUMENT NUMBER: PREV200300101280
TITLE: The chemistry and biology of multivalent saccharide displays.
AUTHOR(S): Mann, David A. [Reprint Author]; **Kiessling, Laura L.** [Reprint Author]
CORPORATE SOURCE: University of Wisconsin-Madison, Madison, WI, USA
SOURCE: Wang, Peng George [Editor, Reprint Author]; Bertozzi, Carolyn R. [Editor]. (2001) pp. 221-275. Glycochemistry: Principles, synthesis, and applications. print.
Publisher: Marcel Dekker AG, Hutgasse 4, CH-4001, Postfach 812, Basel, Switzerland; Marcel Dekker Inc., 270 Madison Avenue, New York, NY, 10016, USA.
ISBN: 0-8247-0538-6 (cloth).
DOCUMENT TYPE: Book; (Book Chapter)
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Feb 2003
Last Updated on STN: 4 Apr 2003

L6 ANSWER 16 OF 53 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:521480 BIOSIS
DOCUMENT NUMBER: PREV200200521480
TITLE: Assembling systems of interacting proteins with synthetic ligands.
AUTHOR(S): **Kiessling, Laura L.** [Reprint author]
CORPORATE SOURCE: Department of Chemistry and Biochemistry, University of Wisconsin-Madison, 1101 University Ave., Madison, WI, 53704, USA
kiessling@chem.wisc.edu
SOURCE: Abstracts of Papers American Chemical Society, (2002) Vol. 224, No. 1-2, pp. ORGN 358. print.
Meeting Info.: 224th National Meeting of the American Chemical Society. Boston, MA, USA. August 18-22, 2002.

CODEN: ACSRAL. ISSN: 0065-7727.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Oct 2002
Last Updated on STN: 9 Oct 2002

L6 ANSWER 17 OF 53 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:490645 BIOSIS
DOCUMENT NUMBER: PREV200200490645
TITLE: Synthesis of sulfated Lewis x polymers and their affinity for L-selectin.
AUTHOR(S): Thomas, William D. [Reprint author]; Owen, Robert M. [Reprint author]; Derda, Ratmir [Reprint author]; Wherritt, Daniel J. [Reprint author]; **Kiessling, Laura L.**
CORPORATE SOURCE: Department of Chemistry, University of Wisconsin, 1101 University Avenue, Madison, WI, 53706, USA
thomas@chem.wisc.edu
SOURCE: Abstracts of Papers American Chemical Society, (2002) Vol. 224, No. 1-2, pp. CARB 96. print.
Meeting Info.: 224th National Meeting of the American Chemical Society. Boston, MA, USA. August 18-22, 2002.
CODEN: ACSRAL. ISSN: 0065-7727.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 18 Sep 2002
Last Updated on STN: 18 Sep 2002

L6 ANSWER 18 OF 53 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:155493 BIOSIS
DOCUMENT NUMBER: PREV200200155493
TITLE: Tuning cellular responses with synthetic, multivalent ligands.
AUTHOR(S): **Kiessling, Laura L.** [Reprint author]
CORPORATE SOURCE: Departments of Chemistry and Biochemistry, University of Wisconsin, 1101 University Avenue, Madison, WI, 53706, USA
SOURCE: Molecular Biology of the Cell, (Dec., 2000) Vol. 11, No. Supplement, pp. 426a. print.
Meeting Info.: 40th American Society for Cell Biology Annual Meeting. San Francisco, CA, USA. December 09-13, 2000. American Society for Cell Biology.
CODEN: MBCEEV. ISSN: 1059-1524.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Feb 2002
Last Updated on STN: 26 Feb 2002

L6 ANSWER 19 OF 53 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:313111 BIOSIS
DOCUMENT NUMBER: PREV200100313111
TITLE: Mechanistic origins of the valency effect: Multivalent **ligand** binding studied by surface plasmon resonance and isothermal titration calorimetry.
AUTHOR(S): Gestwicki, Jason E. [Reprint author]; Cairo, Christopher W. [Reprint author]; Boehm, Frederick J.; **Kiessling, Laura L.**
CORPORATE SOURCE: Department of Biochemistry, University of Wisconsin-Madison, 1101 University Ave., Madison, WI, 53706, USA
gestwicki@biochem.wisc.edu; cairo@chem.wisc.edu
SOURCE: Abstracts of Papers American Chemical Society, (2001) Vol.

221, No. 1-2, pp. MEDI 319. print.
Meeting Info.: 221st National Meeting of the American Chemical Society. San Diego, California, USA. April 01-05, 2001. American Chemical Society.
CODEN: ACSRAL. ISSN: 0065-7727.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English
ENTRY DATE: Entered STN: 4 Jul 2001
Last Updated on STN: 19 Feb 2002

L6 ANSWER 20 OF 53 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:440800 BIOSIS
DOCUMENT NUMBER: PREV200000440800
TITLE: Total synthesis of polymeric 6-sulfo sialyl Lewis x as a multivalent **ligand** for L-selectin.
AUTHOR(S): Yang, Zhi-Qiang [Reprint author]; **Kiessling, Laura L.**
CORPORATE SOURCE: Department of Chemistry, University of Wisconsin, 1101 University Avenue, Madison, WI, 53706, USA
SOURCE: Abstracts of Papers American Chemical Society, (2000) Vol. 220, No. Part 2, pp. ORGN 202. print.
Meeting Info.: 220th National Meeting of the American Chemical Society. Washington, DC, Washington DC, USA. August 20-24, 2000. American Chemical Society.
CODEN: ACSRAL. ISSN: 0065-7727.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English
ENTRY DATE: Entered STN: 18 Oct 2000
Last Updated on STN: 10 Jan 2002

L6 ANSWER 21 OF 53 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:423241 BIOSIS
DOCUMENT NUMBER: PREV199800423241
TITLE: Modulating cell surface protein function with defined, polymeric ligands.
AUTHOR(S): Strong, Laura E. [Reprint author]; Gordon, Eva J. [Reprint author]; Alon, Ronen; **Kiessling, Laura L.** [Reprint author]
CORPORATE SOURCE: Dep Chem., Univ. Wisconsin-Madison, Madison, WI 53706, USA
SOURCE: Abstracts of Papers American Chemical Society, (1998) Vol. 216, No. 1-3, pp. ORGN 439. print.
Meeting Info.: 216th National Meeting of the American Chemical Society. Boston, Massachusetts, USA. August 23-27, 1998. American Chemical Society.
CODEN: ACSRAL. ISSN: 0065-7727.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English
ENTRY DATE: Entered STN: 2 Oct 1998
Last Updated on STN: 2 Oct 1998

L6 ANSWER 22 OF 53 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:238384 BIOSIS
DOCUMENT NUMBER: PREV199800238384
TITLE: Controlling cell surface molecule display with **ligand**-activated proteolysis.
AUTHOR(S): Gordon, Eva J. [Reprint author]; Sanders, William J.; Strong, Laura E.; **Kiessling, Laura L.**
CORPORATE SOURCE: Dep. Chem., Univ. Wis., Madison, WI 53706, USA
SOURCE: Abstracts of Papers American Chemical Society, (1998) Vol. 215, No. 1-2, pp. ORGN 219. print.

Meeting Info.: 215th American Chemical Society National Meeting. Dallas, Texas, USA. March 29-April 2, 1998. American Chemical Society.
CODEN: ACSRAL. ISSN: 0065-7727.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Jun 1998
Last Updated on STN: 4 Jun 1998

L6 ANSWER 23 OF 53 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1997:197297 BIOSIS
DOCUMENT NUMBER: PREV199799496500
TITLE: Multivalent saccharide ligands.
AUTHOR(S): **Kiessling, Laura L.**
CORPORATE SOURCE: Dep. Chem., Univ. Wis., Madison, WI 53706, USA
SOURCE: Abstracts of Papers American Chemical Society, (1997) Vol. 213, No. 1-3, pp. CARB 19.
Meeting Info.: 213th National Meeting of the American Chemical Society. San Francisco, California, USA. April 13-17, 1997.
CODEN: ACSRAL. ISSN: 0065-7727.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 2 May 1997
Last Updated on STN: 2 May 1997

L6 ANSWER 24 OF 53 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1995:422885 BIOSIS
DOCUMENT NUMBER: PREV199598437185
TITLE: Designing modulators of cell-cell interactions: Exploring monovalent and multivalent carbohydrate ligands.
AUTHOR(S): Weatherman, Ross V.; **Kiessling, Laura L.**
CORPORATE SOURCE: Dep. Chem., Univ. Wis.-Madison, 1101 University Ave., Madison, WI 57306, USA
SOURCE: Abstracts of Papers American Chemical Society, (1995) Vol. 210, No. 1-2, pp. ORGN 365.
Meeting Info.: 210th American Chemical Society National Meeting. Chicago, Illinois, USA. August 20-24, 1995.
CODEN: ACSRAL. ISSN: 0065-7727.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Oct 1995
Last Updated on STN: 3 Oct 1995

L6 ANSWER 25 OF 53 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2000183130 EMBASE
TITLE: Synergistic formation of soluble lecfin clusters by a templated multivalent saccharide **ligand** [6].
AUTHOR: Burke S.D.; Zhao Q.; Schuster M.C.; **Kiessling L.L.**
CORPORATE SOURCE: S.D. Burke, Department of Chemistry, University of Wisconsin, Madison, WI 53706, United States
SOURCE: Journal of the American Chemical Society, (10 May 2000) 122/18 (4518-4519).
ISSN: 0002-7863 CODEN: JACSAT
COUNTRY: United States
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English

L6 ANSWER 26 OF 53 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1999290136 EMBASE

TITLE: Scope of multivalent **ligand** function: Lactose-bearing neoglycopolymers by ring-opening metathesis polymerization.

AUTHOR: Pohl N.L.; **Kiessling L.L.**

CORPORATE SOURCE: L.L. Kiessling, Department of Chemistry, University of Wisconsin-Madison, Madison, WI 53706, United States. kiessling@chem.wisc.edu

SOURCE: Synthesis, (1999) -/SPEC. ISS. (1515-1519).
Refs: 23
ISSN: 0039-7881 CODEN: SYNTBF

COUNTRY: Germany

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB A lactose-bearing norbornene imide template was polymerized using (Cy3P)2Cl2Ru=CHPh to produce a lactose-substituted neoglycopolymer. The resulting polymer showed a 100-fold overall increase in inhibitory potency (5-fold increase on a per saccharide residue basis) compared to monomeric lactose in both a galectin-binding assay and an Erythrina corallodendrum hemagglutination assay.

L6 ANSWER 27 OF 53 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1999247372 EMBASE

TITLE: A general synthetic route to defined, biologically active multivalent arrays.

AUTHOR: Strong L.E.; **Kiessling L.L.**

CORPORATE SOURCE: L.L. Kiessling, Department of Chemistry, University of Wisconsin, Madison, WI 53706, United States

SOURCE: Journal of the American Chemical Society, (7 Jul 1999) 121/26 (6193-6196).
ISSN: 0002-7863 CODEN: JACSAT

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB A new, general strategy for the synthesis of biologically active multivalent arrays displaying diverse functionality has been developed. This method exploits the ability of ring-opening metathesis polymerizations to produce polymers of defined lengths. By incorporating N-hydroxysuccinimide esters into the polymers, recognition epitopes bearing nucleophilic functional groups, in this case an α-mannose derivative, can be attached. The synthesis, characterization, and biological evaluation of mannose- beating polymers demonstrated the utility of this new methodology. This strategy will facilitate the creation of diverse multivalent libraries and the large-scale production of multidentate ligands.

L6 ANSWER 28 OF 53 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1998369028 EMBASE

TITLE: Probing low affinity and multivalent interactions with surface plasmon resonance: Ligands for concanavalin A.

AUTHOR: Mann D.A.; Kanai M.; Maly D.J.; **Kiessling L.L.**

CORPORATE SOURCE: L.L. Kiessling, Department of Chemistry, University of Wisconsin, Madison, WI 53706, United States

SOURCE: Journal of the American Chemical Society, (21 Oct 1998) 120/41 (10575-10582).

ISSN: 0002-7863 CODEN: JACSAT
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The affinities of the carbohydrate-binding protein concanavalin A (Con A) for mono- and multivalent ligands were measured by surface plasmon resonance (SPR) detection. Assessing protein-carbohydrate affinities is typically difficult due to weak affinities observed and the complications that arise from the importance of multivalency in these interactions. We describe a convenient method to rapidly evaluate the inhibitory constants for a panel of different ligands, both monovalent and multivalent, for low- affinity receptors, such as the carbohydrate-binding protein Con A. A nonnatural, mannose-substituted glycolipid was synthesized, and self-assembled monolayers of varying carbohydrate density were generated. The synthetic surfaces bind Con A. Competition experiments that employed monovalent ligands in solution yielded K(i) values similar to equilibrium binding constants obtained in titration microcalorimetry experiments. In addition, this assay could be used to examine various polymeric ligands of defined lengths, generated by ring-opening metathesis polymerization (ROMP). This study demonstrates the utility of this method for rapidly screening ligands that engage in low affinity interactions with their target receptors. Our results emphasize that those molecules that can simultaneously occupy two or more saccharide binding sites within a lectin oligomer are effective inhibitors of protein-carbohydrate interactions.

L6 ANSWER 29 OF 53 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1998108636 EMBASE
TITLE: Synthetic ligands point to cell surface strategies [8].
AUTHOR: Gordon E.J.; Sanders W.J.; **Kiessling L.L.**
CORPORATE SOURCE: E.J. Gordon, Department of Chemistry/Biochemistry, University of Wisconsin, Madison, WI 53706, United States. kiessling@chem.wisc.edu
SOURCE: Nature, (5 Mar 1998) 392/6671 (30-31).
Refs: 10
ISSN: 0028-0836 CODEN: NATUAS
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English

L6 ANSWER 30 OF 53 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 97336027 EMBASE
DOCUMENT NUMBER: 1997336027
TITLE: Varying the size of multivalent ligands: The dependence of concanavalin A binding on neoglycopolymer length.
AUTHOR: Kanai M.; Mortell K.H.; **Kiessling L.L.**
CORPORATE SOURCE: L.L. Kiessling, Department of Chemistry, University of Wisconsin, Madison, WI 53706, United States
SOURCE: Journal of the American Chemical Society, (1997) 119/41 (9931-9932).
Refs: 21
ISSN: 0002-7863 CODEN: JACSAT
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
LANGUAGE: English

L6 ANSWER 31 OF 53 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2001:658628 SCISEARCH

THE GENUINE ARTICLE: 434PJ
TITLE: Mechanistic origins of the valency effect: Multivalent **ligand** binding studied by surface plasmon resonance and isothermal titration calorimetry.
AUTHOR: Gestwicki J E (Reprint); Cairo C W; Boehm F J; **Kiessling L L**
CORPORATE SOURCE: Univ Wisconsin, Dept Biochem, Madison, WI 53706 USA; Univ Wisconsin, Madison, WI 53706 USA; Univ Wisconsin, Dept Chem, Madison, WI 53706 USA
COUNTRY OF AUTHOR: USA
SOURCE: ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY, (1 APR 2001) Vol. 221, Part 2, pp. U56-U56. MA 319-MEDI.
Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA.
ISSN: 0065-7727.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0

L6 ANSWER 32 OF 53 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2001:131046 SCISEARCH
THE GENUINE ARTICLE: 386XV
TITLE: Total synthesis of polymeric 6-sulfo sialyl Lewis X as a multivalent **ligand** for L-selectin.
AUTHOR: Yang Z Q (Reprint); **Kiessling L L**
CORPORATE SOURCE: Univ Wisconsin, Dept Chem, Madison, WI 53706 USA; Univ Wisconsin, Dept Biochem, Madison, WI 53705 USA
COUNTRY OF AUTHOR: USA
SOURCE: ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY, (20 AUG 2000) Vol. 220, Part 2, pp. U64-U64. MA 202-ORGN.
Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA.
ISSN: 0065-7727.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0

L6 ANSWER 33 OF 53 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2001:11187 SCISEARCH
THE GENUINE ARTICLE: 386CK
TITLE: Visualization of single multivalent receptor-**ligand** complexes by transmission electron microscopy
AUTHOR: Gestwicki J E; Strong L E; **Kiessling L L (Reprint)**
CORPORATE SOURCE: Univ Wisconsin, Dept Chem, 1101 Univ Ave, Madison, WI 53706 USA (Reprint); Univ Wisconsin, Dept Chem, Madison, WI 53706 USA; Univ Wisconsin, Dept Biochem, Madison, WI 53706 USA
COUNTRY OF AUTHOR: USA
SOURCE: ANGEWANDTE CHEMIE-INTERNATIONAL EDITION, (JAN 2000) Vol. 39, No. 24, pp. 4567-+.
Publisher: WILEY-V C H VERLAG GMBH, PO BOX 10 11 61, D-69451 BERLIN, GERMANY.
ISSN: 1433-7851.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 25

L6 ANSWER 34 OF 53 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2000:836328 SCISEARCH
THE GENUINE ARTICLE: BQ93T
TITLE: Principles for multivalent **ligand** design
AUTHOR: **Kiessling L L (Reprint)**; Strong L E; Gestwicki J

E
CORPORATE SOURCE: UNIV WISCONSIN, DEPT CHEM, 1101 UNIV AVE, MADISON, WI 53706 (Reprint); UNIV WISCONSIN, DEPT BIOCHEM, MADISON, WI 53706
COUNTRY OF AUTHOR: USA
SOURCE: ANNUAL REPORTS IN MEDICINAL CHEMISTRY, (MAR-APR 2000) Vol. 35, pp. 321-330.
Publisher: ACADEMIC PRESS INC, 525 B STREET, SUITE 1900, SAN DIEGO, CA 92101-4495.
ISSN: 0065-7743.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 26

L6 ANSWER 35 OF 53 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 1998:210238 SCISEARCH
THE GENUINE ARTICLE: ZA912
TITLE: Controlling cell surface molecule display with **ligand**-activated proteolysis.
AUTHOR: Gordon E J (Reprint); Sanders W J; Strong L E; **Kiessling L L**
CORPORATE SOURCE: UNIV WISCONSIN, DEPT CHEM, MADISON, WI 53706; UNIV WISCONSIN, DEPT BIOCHEM, MADISON, WI 53706
COUNTRY OF AUTHOR: USA
SOURCE: ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY, (2 APR 1998) Vol. 215, Part 2, pp. 219-ORGN.
Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036.
ISSN: 0065-7727.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0

L6 ANSWER 36 OF 53 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 93:476165 SCISEARCH
THE GENUINE ARTICLE: LP322
TITLE: SYNTHESIS OF SIALYL LEWIS-X AS A **LIGAND** FOR STUDIES WITH E-SELECTIN
AUTHOR: POHL N L (Reprint); MANNING D D; **KIESSLING L L**
CORPORATE SOURCE: UNIV WISCONSIN, DEPT CHEM, MADISON, WI, 53706
COUNTRY OF AUTHOR: USA
SOURCE: ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY, (22 AUG 1993) Vol. 206, Part 2, pp. 60-ORGN.
ISSN: 0065-7727.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: ENGLISH
REFERENCE COUNT: No References

L6 ANSWER 37 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:979831 CAPLUS
TITLE: Synthetic multivalent carbohydrate ligands as effectors or inhibitors of biological processes
AUTHOR(S): **Kiessling, Laura L.**; Pontrello, Jason K.; Schuster, Michael C.
CORPORATE SOURCE: Germany
SOURCE: Carbohydrate-Based Drug Discovery (2003), Volume 2, 575-608. Editor(s): Wong, Chi-Huey. Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, Germany.
CODEN: 69EWXA; ISBN: 3-527-30632-3
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review discusses how **ligand**, in particular synthetic

multivalent carbohydrate **ligand**, influences inhibitor or effector function. Systematic variations in **ligand** structure can result in the production of potent ligands, even when the protein target is not well characterized. Effector ligands able to regulate biol. responses can be used to illuminate the mechanisms of signal transduction.

REFERENCE COUNT: 99 THERE ARE 99 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 38 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:658058 CAPLUS
DOCUMENT NUMBER: 140:5446
TITLE: Synthesis and binding mechanisms of polymeric multivalent ligands
AUTHOR(S): **Kiessling, Laura L.**
CORPORATE SOURCE: Departments of Chemistry and Biochemistry, University of Wisconsin-Madison, Madison, WI, 53706, USA
SOURCE: Polymer Preprints (American Chemical Society, Division of Polymer Chemistry) (2003), 44(2), 447-448
CODEN: ACPPAY; ISSN: 0032-3934
PUBLISHER: American Chemical Society, Division of Polymer Chemistry
DOCUMENT TYPE: Journal; (computer optical disk)
LANGUAGE: English

AB We have generated diverse collection of multivalent ligands and tested in variety of assays to elucidate multivalence bonding mechanisms. Multivalent ligands generated from different scaffolds function by different mechanisms.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 39 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:181414 CAPLUS
TITLE: Design and fabrication of surfaces for the combinatorial exploration of cell adherence and differentiation
AUTHOR(S): Derda, Ratmir; Orner, Brendan P.; **Kiessling, Laura L.**
CORPORATE SOURCE: Department of Chemistry, University of Wisconsin, Madison, WI, 53706, USA
SOURCE: Abstracts of Papers, 225th ACS National Meeting, New Orleans, LA, United States, March 23-27, 2003 (2003), COLL-311. American Chemical Society: Washington, D. C.
CODEN: 69DSA4
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB Arrays of compds. can be screened to identify ligands that promote cell adhesion, differentiation or signaling. Such ligands can be used to address fundamental cell biol. questions. A **ligand** chip presenting arrays of mols. designed to bind cell surface receptors must be fabricated such that the individual compds. displayed are spatially isolated. The regions of the surface that do not display specific ligands must resist not only cell adhesion but also solution spreading, such that cross-contamination during array production is avoided. Although self assembled monolayers consisting of perfluorinated mols. have been shown to nonspecifically adsorb proteins, they prevent the nonspecific attachment and spreading of cells. We have found that multiple cell lines can be patterned using surfaces modified with adhesive and non-adhesive perfluorinated groups. These designed surfaces are suitable for generating compound arrays due to the ability of the perfluorinated regions to resist the spreading of a wide range of solvents.

L6 ANSWER 40 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:775508 CAPLUS
TITLE: Assembling systems of interacting proteins with synthetic ligands
AUTHOR(S): **Kiessling, Laura L.**
CORPORATE SOURCE: Departments of Chemistry and Biochemistry, University of Wisconsin-Madison, Madison, WI, 53704, USA
SOURCE: Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002 (2002), ORGN-358. American Chemical Society: Washington, D. C.
CODEN: 69CZPZ
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Chemical synthesis offers many approaches to investigate the combinatorial interactions of proteins encoded by genomes. Protein - protein interactions are essential to many processes, including signal transduction. Ligands that mediate the assembly of defined multi-protein complexes on the cell surface can activate or inhibit signaling pathways depending on how many and which proteins are engaged. We have developed methods for the syntheses of diverse multivalent ligands, which display binding elements that for cell-surface proteins. The resulting compds. have been used to investigate the consequences of protein clustering for a range of distinct cellular processes. For example, multivalent ligands have been used to elucidate the mechanisms by which bacteria amplify the signals that elicit chemotaxis. We also have used multivalent **ligand** binding to regulate B cell activation, a process that is essential in generating vaccines and controlling autoimmune responses. Our recent results on multivalent **ligand** synthesis and function will be discussed.

L6 ANSWER 41 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:614409 CAPLUS
TITLE: Chemical approaches to eliciting and inhibiting immune responses
AUTHOR(S): **Kiessling, Laura L.**
CORPORATE SOURCE: Departments of Chemistry and Biochemistry, University of Wisconsin, Madison, WI, 53706, USA
SOURCE: Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002 (2002), CARB-080. American Chemical Society: Washington, D. C.
CODEN: 69CZPZ
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB To promote selective immune responses to carbohydrate epitopes, multivalent carbohydrate ligands that can bind and cluster the B cell antigen receptor (BCR) are typically used. By clustering the BCR, ligands can elicit signals that lead to the promotion of antibody production (i.e., function as a vaccine) or inhibition of antibody production (i.e., function as a selective immunosuppressant). The output response depends on many factors including the structure and the valency of the multivalent **ligand.** We have begun to synthesize multivalent ligands with differing structural features to examine how **ligand** structure influences the output responses of B cells. Our long-term objective is to identify ligands that selectively promote or inhibit the production of specific antibodies. Our initial results directed toward this goal will be discussed.

L6 ANSWER 42 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:713652 CAPLUS
DOCUMENT NUMBER: 135:271869
TITLE: Methods and reagents for regulation of cellular responses in biological systems

INVENTOR(S): **Kiessling, Laura L.**; Strong, Laura E.; Gestwicki, Jason E.
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001071309	A2	20010927	WO 2001-US9174	20010321
WO 2001071309	A3	20030515		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001081499	A5	20011003	AU 2001-81499	20010321
US 2003125262	A1	20030703	US 2001-815296	20010321
EP 1334118	A2	20030813	EP 2001-959934	20010321
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004512258	T2	20040422	JP 2001-569247	20010321

PRIORITY APPLN. INFO.: US 2000-191014P P 20000321
WO 2001-US9174 W 20010321

AB This invention provides multivalent ligands which carry or display at least one recognition element (RE), and preferably a plurality of recognition elements, for binding directly or indirectly to cells or other biol. particles or more generally by binding to any biol. mol. The multivalent ligands provided can most generally function for binding or targeting to any biol. particle or mol. and particularly to targeting of cells or cell types or viruses, for cell aggregation and generally for macromol. assembly of biol. macromoleculares. The multivalent ligands of this invention are generally applicable for creating scaffolds (assemblies) of chemical or biol. species, including without limitation, antigens, epitopes, **ligand** binding groups, ligands for cell receptors (cell surface receptors, transmembrane receptors and cytoplasmic receptors), various macromols. (nucleic acids, carbohydrates, saccharides, proteins, peptides, etc.). In these scaffolds, the number, spacing, relative positioning and relative orientation of recognition elements can be controlled. Multivalent ligands of this invention can carry or display at least one signal recognition element (SRE), and preferably a plurality of signal recognition elements, and modulate biol. responses in biol. systems. The invention also relates to methods for aggregating biol. particles and macromols. and for modulating biol. response employing the multivalent ligands provided.

L6 ANSWER 43 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:202226 CAPLUS
TITLE: Mechanistic origins of the valency effect: Multivalent **ligand** binding studied by surface plasmon resonance and isothermal titration calorimetry
AUTHOR(S): Gestwicki, Jason E.; Cairo, Christopher W.; Boehm, Frederick J.; **Kiessling, Laura L.**
CORPORATE SOURCE: Department of Biochemistry, University of Wisconsin-Madison, Madison, WI, 53706, USA
SOURCE: Abstracts of Papers - American Chemical Society

(2001), 221st, MEDI-319
CODEN: ACSRAL; ISSN: 0065-7727
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; Meeting Abstract
LANGUAGE: English
AB Functional affinity describes the apparent affinity of a multivalent **ligand** for its corresponding receptor(s). It has been shown in many systems that increasing the valency of a **ligand** improves its functional affinity. These changes in functional affinity are exploited by biol. systems to enhance the binding of cell surface receptors and antibodies. Various mechanisms have been invoked to describe the origins of this "valency effect". These include statistical effects, receptor crosslinking, and chelation. The relative contribution of these mechanisms to functional affinity, however, have proven to be difficult to determine We have generated a series of carbohydrate ligands varying systematically in structural features and studied their interaction with the tetrameric receptor, Con A (Con A) by a number of exptl. approaches. We address the mechanistic origins of the "valency effect" by a combination of our choice of **ligand**-receptor pair and through exptl. design. These studies are directed at developing a better fundamental understanding of multivalent interactions important to biol.

L6 ANSWER 44 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:796704 CAPLUS
TITLE: Total synthesis of polymeric 6-sulfo sialyl Lewis x as a multivalent **ligand** for L-selectin.
AUTHOR(S): Yang, Zhi-Qiang; **Kiessling, Laura L.**
CORPORATE SOURCE: Department of Chemistry, University of Wisconsin, Madison, WI, 53706, USA
SOURCE: Abstracts of Papers - American Chemical Society (2000), 220th, ORGN-202
CODEN: ACSRAL; ISSN: 0065-7727
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; Meeting Abstract
LANGUAGE: English
AB One of the physiol. ligands of L-selectin, GlyCAM-1, is a mucin with sulfated, sialylated and fucosylated oligosaccharide sequences. This glycoprotein presents multiple displays of a sulfated tetrasaccharide, 6-sulfo sialyl Lewis x (6-sulfo sLex, 1) recognition epitope on an extended polypeptide backbone. In our effort to search for high affinity, specific inhibitors for L-selectin-**ligand** interactions, we synthesized a neoglycopolymer (2) displaying multiple copies of 6-sulfo sLex. This polymer, which was generated using the ring-opening metathesis polymerization (ROMP), shares critical common features with natural L-selectin ligands.

L6 ANSWER 45 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:542705 CAPLUS
TITLE: Exploring receptor interactions with materials generated via metathesis reactions.
AUTHOR(S): Strong, Laura E.; Gestwicki, Jason E.; **Kiessling, Laura L.**
CORPORATE SOURCE: Department of Chemistry, University of Wisconsin-Madison, Madison, WI, 53706, USA
SOURCE: Book of Abstracts, 218th ACS National Meeting, New Orleans, Aug. 22-26 (1999), ORGN-324. American Chemical Society: Washington, D. C.
CODEN: 67ZJA5
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Cell surface binding interactions are involved in a wide variety of biol. phenomena, including the ability of organisms to sense their surroundings. Many types of mols., including peptides and carbohydrates, are

specifically recognized in receptor-**ligand** interactions at cell surfaces. The physiol. relevant display of recognition epitopes is not straightforward to determine Yet, variations in **ligand** presentation can have a major impact, not only on receptor-**ligand** binding, but also on downstream effects such as signal transduction. Chemical synthesis provides tools that can illuminate these biol. pathways. In order to gain a more in depth understanding of cell surface interactions, we have developed a new, generalizable method for the synthesis of multidentate ligands using metathesis reactions. This chemical has allowed us to generate a series of biol. active ligands, which have been used to study both eukaryotic and prokaryotic recognition and signaling events. In addition, this method is flexible enough for the preparation of diverse libraries of ligands.

L6 ANSWER 46 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:145753 CAPLUS
TITLE: Tuning cellular responses with synthetic, multivalent ligands
AUTHOR(S): **Kiessling, Laura L.**
CORPORATE SOURCE: Departments of Chemistry and Biochemistry, University of Wisconsin, Madison, WI, 53706, USA
SOURCE: Book of Abstracts, 217th ACS National Meeting, Anaheim, Calif., March 21-25 (1999), ORGN-320. American Chemical Society: Washington, D. C. CODEN: 67GHA6
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Signaling initiated by the clustering of extracellular proteins is one mechanism cells use to respond to their environment. For example, bacteria react with exquisite sensitivity to low concns. of attractants, such as galactose, yet they also detect concentration gradients of attractants over a range of 5 orders of magnitude. How do cells tune their signals. Specifically, how can they respond to mols. in their environment with both high sensitivity and a broad dynamic range. We hypothesized that the extent of cell surface protein clustering could alter the magnitude of a resulting signal. We used chemical synthesis to test this hypothesis: Applying living ring-opening metathesis polymerization reactions, we created galactose-substituted oligomers of different valencies that could cluster galactose receptors to different extents. Our studies reveal that the magnitude of a signal can depend strongly on the ability of the **ligand** to induce protein clustering, and that synthetic ligands can be used to modulate as well as initiate signal transduction.

L6 ANSWER 47 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:66775 CAPLUS
DOCUMENT NUMBER: 130:292844
TITLE: The molecular recognition of saccharides and glycoprotein-inspired materials
AUTHOR(S): **Kiessling, L. L.**
CORPORATE SOURCE: Departments of Chemistry and Biochemistry, University of Wisconsin, Madison, WI, 53706, USA
SOURCE: Ernst Schering Research Foundation Workshop (1998), 26(Recent Trends in Molecular Recognition), 183-212 CODEN: ESRWEL; ISSN: 0947-6075
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 70 refs. Although it is not well understood, multivalent binding is critical in physiol. settings. Cell adhesion, antibody-antigen recognition, and some signal transduction events rely on multi-point receptor-**ligand** interactions to produce the proper response. We have found that emerging techniques in organometallic and polymer chemical can be used to study these complex, yet fundamental problems in biomol.

recognition. Our studies indicate that several factors contribute to the high functional affinities often observed in multivalent recognition events. For example, oligomeric or membrane-associated proteins that bind natural multivalent saccharide displays may benefit from the high local concentration of recognition epitopes presented through glycoprotein or glycolipid clusters. In these configurations, both the effects of decreased off-rates and multi-point binding can contribute to the functional affinities observed in the interactions. Addnl. investigations will illuminate further the mol. mechanisms that give rise to affinity and specificity in such systems.

REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 48 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:530801 CAPLUS

TITLE: Modulating cell surface protein function with defined, polymeric ligands.

AUTHOR(S): Strong, Laura E.; Gordon, Eva J.; Alon, Ronen; **Kiessling, Laura L.**

CORPORATE SOURCE: Weizmann Institute Science, University Wisconsin, Madison, WI, 53706, USA

SOURCE: Book of Abstracts, 216th ACS National Meeting, Boston, August 23-27 (1998), ORGN-439. American Chemical Society: Washington, D. C.
CODEN: 66KYA2

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB Neoglycopolymers were designed to mimic natural ligands for the selectins, a family of carbohydrate-binding proteins that mediate leukocyte rolling, an initial step in the inflammatory response. Sulfation and glycosylation of the L-selectin **ligand** GlyCAM-1 is necessary for binding; therefore sulfated, carbohydrate-bearing polymers were generated using ring opening metathesis polymerization (ROMP). ROMP methodol. is ideal for the synthesis of biomimetic polymers due to the ability to control polymer length, the tolerance of functionality, and the potential to generate block copolymers. The biol. activity of this material was assessed in two assays. First, it was determined that the neoglycopolymer inhibited cell rolling in a dose-dependent manner. These results are significant because L-selectin mediates the rolling of white blood cells along the inflamed blood vessel wall. In light of recent evidence that L-selectin is proteolytically cleaved from the cell surface during cell rolling, we investigated whether multivalent ligands with potential to cluster L-selectin could also induce this cleavage. When human neutrophils were incubated with the neoglycopolymer, a dose-dependent loss of L-selectin from the cell surface was observed These results demonstrate that readily assembled materials can be used not only to modulate biomol. recognition but to control the presence of proteins on the cell surface.

L6 ANSWER 49 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:139736 CAPLUS

TITLE: Controlling cell surface molecule display with **ligand**-activated proteolysis.

AUTHOR(S): Gordon, Eva J.; Sanders, William J.; Strong, Laura E.; **Kiessling, Laura L.**

CORPORATE SOURCE: Department Chemistry, University Wisconsin, Madison, WI, 53706, USA

SOURCE: Book of Abstracts, 215th ACS National Meeting, Dallas, March 29-April 2 (1998), ORGN-219. American Chemical Society: Washington, D. C.
CODEN: 65QTAA

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB The proteolytic release, or shedding, of a cell surface protein can serve a regulatory role; the process liberates a soluble form of the protein into circulation while down regulating its cell surface concentration A diverse group of proteins including cell adhesion mols., cytokines and cytokine receptors, growth factors and growth factor receptors are released from the cell surface. The characteristics that render a protein susceptible to proteolytic cleavage are not known. We hypothesized that the clustering of a protein at the cell surface might target it for proteolysis. To test this hypothesis, synthetic, multivalent ligands have been designed that can bind the adhesion protein L-selectin. That these materials selectively promote the proteolytic release of L-selectin has now been demonstrated. Because mols. that control receptor shedding can be used to alter cellular responsiveness to specific ligands or to promote responses at distal sites, these results have broad implications for regulating the location and presentation of important biomols.

L6 ANSWER 50 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:488424 CAPLUS
TITLE: Synthesis of lactose polymers for the galectins by ring-opening metathesis polymerization.
AUTHOR(S): Pohl, Nicola L.; Leffler, Hakon; **Kiessling, Laura L.**
CORPORATE SOURCE: Department Chemistry, University Wisconsin, Madison, WI, 53706, USA
SOURCE: Book of Abstracts, 214th ACS National Meeting, Las Vegas, NV, September 7-11 (1997), ORGN-020. American Chemical Society: Washington, D. C.
CODEN: 64RNAO
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB New ligands targeted to the saccharide-binding site of the galectins were synthesized to assay the degree of enhancement that a polymeric **ligand** has over monomeric ligands on galectin inhibition. Acylated lactose was attached to a norbornene template via a Mitsunobu reaction of an alc. linker. This template was deacylated and then underwent ring opening metathesis polymerization with Cl2(Cy3P)2Ru=C(H)Ph as the catalyst. The resulting polymer was tested against two galectins-Gal-1 and Gal-3, with the corresponding mannose polymer and monovalent lactose as controls.

L6 ANSWER 51 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:158952 CAPLUS
TITLE: Multivalent saccharide ligands
AUTHOR(S): **Kiessling, Laura L.**
CORPORATE SOURCE: Department Chemistry, University Wisconsin, Madison, WI, 53706, USA
SOURCE: Book of Abstracts, 213th ACS National Meeting, San Francisco, April 13-17 (1997), CARB-019. American Chemical Society: Washington, D. C.
CODEN: 64AOAA
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB A critical feature that distinguishes cell surface protein-saccharide recognition events from receptor-**ligand** interactions in solution is that the former often benefit from multivalent binding. The syntheses and applications of synthetic multidentate ligands to elucidate structure and function relationships in protein - saccharide interactions will be presented. Using information from studies of both monovalent and multivalent carbohydrate derivs., selective ligands that target physiol. relevant proteins, such as the selectins, have been generated. These multivalent saccharide derivs. can function as more than inhibitors: they

can promote specific cellular processes, including the shedding of cell surface L-selectin.

L6 ANSWER 52 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:220989 CAPLUS
TITLE: Structure-function studies on neoglycopolymers produced by aqueous ring-opening metathesis polymerization.
AUTHOR(S): Mortell, Kathleen H.; Schuster, Michael C.; **Kiessling, Laura L.**
CORPORATE SOURCE: Department Chemistry, University Wisconsin, Madison, 53706, USA
SOURCE: Book of Abstracts, 211th ACS National Meeting, New Orleans, LA, March 24-28 (1996), ORGN-385. American Chemical Society: Washington, D. C.
CODEN: 62PIAJ
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Non-natural carbohydrate-bearing polymers have emerged as promising materials for the study of cell adhesion mediated by multivalent carbohydrate-protein interactions. The present study investigates how saccharide structure, polymer structure and saccharide residue d. affect neoglycopolymer-protein binding. Neoglycopolymers were generated using a ruthenium-catalyzed ring-opening metathesis polymerization in aqueous solution The polymerization occurs in protic media and tolerates functionalized monomers bearing unprotected carbohydrates. Polymerization reactions were initiated with various catalyst species, and the resulting polymer structures were characterized by 1H and 13C NMR. The polymers were tested for their ability to act as ligands for a glucose mannose binding protein, Con A. Polymers carrying a single sugar **ligand** per repeat unit were found to be more potent inhibitors of Con A-mediated hemagglutination than polymers carrying two sugars per repeat unit.

L6 ANSWER 53 OF 53 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:924979 CAPLUS
TITLE: Designing modulators of cell-cell interactions: Exploring monovalent and multivalent carbohydrate ligands.
AUTHOR(S): Weatherman, Ross V.; **Kiessling, Laura L.**
CORPORATE SOURCE: Department Chemistry, University Wisconsin, Madison, WI, 53706, USA
SOURCE: Book of Abstracts, 210th ACS National Meeting, Chicago, IL, August 20-24 (1995), Issue Pt. 2, ORGN-365. American Chemical Society: Washington, D. C.
CODEN: 61XGAC
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB The Con A -carbohydrate interaction was used as a model to elucidate the principles for designing effective monovalent and multivalent inhibitors of carbohydrate-mediate cell adhesion. This system provides a good model in which to compare well-characterized monvalent inhibitors with multivalent carbohydrate polymers recently developed in this laboratory A fluorescence anisotropy assay was developed to quantitate the binding of monovalent carbohydrates to Con A. Fluorescein-labeled derivs. of mannose and glucose were synthesized and used as ligands in the assay. Competition expts. with monosaccharides gave similar binding energies as those obtained using microcalorimetry. The interaction of Con A with multivalent carbohydrate polymers was characterized using hemagglutination assays. Of particular interest was how the differences in monovalent binding affinity for mannose and glucose would be effected upon making the

ligand multivalent. Kinetics studies showed a greater difference between the inhibitory doses of the two polymers at short time points than at longer time points, The effect of polymer length and spacing between ligands will also be investigated. A general model for multivalent **ligand** binding incorporating these results will be proposed.

```
=> s receptor
   3 FILES SEARCHED...
L7     2917765 RECEPTOR

=> s l7 and ligand
L8      270426 L7 AND LIGAND

=> s l8 and multivalent(a)ligand
L9          271 L8 AND MULTIVALENT(A) LIGAND

=> s l9 and (scaffold or array)
L10          12 L9 AND (SCAFFOLD OR ARRAY)

=> dup rem
ENTER L# LIST OR (END):l10
PROCESSING COMPLETED FOR L10
L11            6 DUP REM L10 (6 DUPLICATES REMOVED)

=> d ti 1-6

L11  ANSWER 1 OF 6     MEDLINE on STN                    DUPLICATE 1
TI   Influencing receptor-ligand binding mechanisms with
     multivalent ligand architecture.

L11  ANSWER 2 OF 6  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Cell Aggregation by Scaffolded Receptor Clusters

L11  ANSWER 3 OF 6  CAPLUS  COPYRIGHT 2004 ACS on STN  DUPLICATE 2
TI   Methods and reagents for regulation of cellular responses in biological
     systems

L11  ANSWER 4 OF 6  BIOSIS  COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
TI   Tuning cellular responses with synthetic, multivalent ligands.

L11  ANSWER 5 OF 6     MEDLINE on STN                    DUPLICATE 3
TI   Monitoring antigen-specific T cells using MHC-Ig dimers.

L11  ANSWER 6 OF 6  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Multivalent, but not divalent, antigen receptor cross-linkers
     synergize with CD40 ligand for induction of Ig synthesis and
     class switching in normal murine B cells. A redefinition of the TI-2 vs T
     cell-dependent antigen dichotomy


=> d l10 ibib abs 1-6

L10  ANSWER 1 OF 12     MEDLINE on STN
ACCESSION NUMBER:    2002713567     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 12475334
TITLE:               Influencing receptor-ligand binding
                     mechanisms with multivalent ligand
                     architecture.
AUTHOR:              Gestwicki Jason E; Cairo Christopher W; Strong Laura E;
                     Oetjen Karolyn A; Kiessling Laura L
CORPORATE SOURCE:    Departments of Biochemistry and Chemistry, University of
                     Wisconsin-Madison, Madison, WI 53706, USA.
```

CONTRACT NUMBER: GM 08349 (NIGMS)
GM 18750 (NIGMS)
GM 49975 (NIGMS)
SOURCE: Journal of the American Chemical Society, (2002 Dec 18) 124 (50) 14922-33.
Journal code: 7503056. ISSN: 0002-7863.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20021217
Last Updated on STN: 20030308
Entered Medline: 20030307

AB Multivalent ligands can function as inhibitors or effectors of biological processes. Potent inhibitory activity can arise from the high functional affinities of **multivalent ligand-receptor** interactions. Effector functions, however, are influenced not only by apparent affinities but also by alternate factors, including the ability of a **ligand** to cluster receptors. Little is known about the molecular features of a **multivalent ligand** that determine whether it will function as an inhibitor or effector. We envisioned that, by altering **multivalent ligand** architecture, ligands with preferences for different binding mechanisms would be generated. To this end, a series of 28 ligands possessing structural diversity was synthesized. This series provides the means to explore the effects of **ligand** architecture on the inhibition and clustering of a model protein, the lectin concanavalin A (Con A). The structural parameters that were varied include **scaffold** shape, size, valency, and density of binding elements. We found that ligands with certain architectures are effective inhibitors, but others mediate **receptor** clustering. Specifically, high molecular weight, polydisperse polyvalent ligands are effective inhibitors of Con A binding, whereas linear oligomeric ligands generated by the ring-opening metathesis polymerization have structural properties that favor clustering. The shape of a **multivalent ligand** also influences specific aspects of **receptor** clustering. These include the rate at which the **receptor** is clustered, the number of receptors in the clusters, and the average interreceptor distance. Our results indicate that the architecture of a **multivalent ligand** is a key parameter in determining its activity as an inhibitor or effector. Diversity-oriented syntheses of multivalent ligands coupled with effective assays that can be used to compare the contributions of different binding parameters may afford ligands that function by specific mechanisms.

L10 ANSWER 2 OF 12 MEDLINE on STN
ACCESSION NUMBER: 2000412569 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10854185
TITLE: Monitoring antigen-specific T cells using MHC-Ig dimers.
AUTHOR: Schneck J P
CORPORATE SOURCE: Johns Hopkins University, School of Medicine, Department of Oncology, Baltimore, Maryland, USA.
SOURCE: Immunological investigations, (2000 May) 29 (2) 163-9.
Journal code: 8504629. ISSN: 0882-0139.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000907
Last Updated on STN: 20000907
Entered Medline: 20000825

AB To summarize, two novel approaches are currently being examined that allow

for identification of antigen-specific T cells. A biochemical approach to generating soluble multivalent MHC complexes has been to generate tetrameric MHC complexes linked to avidin. We have also generated a general approach for producing soluble divalent versions of class I and class II MHC molecules, using Ig as a molecular **scaffold**. The experimental system described here outlines a general approach of using multivalent high affinity ligands to study cell-cell interactions, driven by **multivalent ligand-receptor** interactions.
Our work indicates that divalent chimeric molecules are high-avidity analogs of proteins useful in probing and selectively regulating cellular responses.

L10 ANSWER 3 OF 12 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:121112 BIOSIS
DOCUMENT NUMBER: PREV200300121112
TITLE: Influencing **receptor-ligand** binding mechanisms with **multivalent ligand** architecture.
AUTHOR(S): Gestwicki, Jason E.; Cairo, Christopher W.; Strong, Laura E.; Oetjen, Karolyn A.; Kiessling, Laura L. [Reprint Author]
CORPORATE SOURCE: Department of Biochemistry, University of Wisconsin-Madison, Madison, WI, 53706, USA
kiessling@chem.wisc.edu
SOURCE: Journal of the American Chemical Society, (December 18 2002) Vol. 124, No. 50, pp. 14922-14933. print.
ISSN: 0002-7863 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Mar 2003
Last Updated on STN: 5 Mar 2003

AB Multivalent ligands can function as inhibitors or effectors of biological processes. Potent inhibitory activity can arise from the high functional affinities of **multivalent ligand-receptor** interactions. Effector functions, however, are influenced not only by apparent affinities but also by alternate factors, including the ability of a **ligand** to cluster receptors. Little is known about the molecular features of a **multivalent ligand** that determine whether it will function as an inhibitor or effector. We envisioned that, by altering **multivalent ligand** architecture, ligands with preferences for different binding mechanisms would be generated. To this end, a series of 28 ligands possessing structural diversity was synthesized. This series provides the means to explore the effects of **ligand** architecture on the inhibition and clustering of a model protein, the lectin concanavalin A (Con A). The structural parameters that were varied include **scaffold** shape, size, valency, and density of binding elements. We found that ligands with certain architectures are effective inhibitors, but others mediate **receptor** clustering. Specifically, high molecular weight, polydisperse polyvalent ligands are effective inhibitors of Con A binding, whereas linear oligomeric ligands generated by the ring-opening metathesis polymerization have structural properties that favor clustering. The shape of a **multivalent ligand** also influences specific aspects of **receptor** clustering. These include the rate at which the **receptor** is clustered, the number of receptors in the clusters, and the average interreceptor distance. Our results indicate that the architecture of a **multivalent ligand** is a key parameter in determining its activity as an inhibitor or effector. Diversity-oriented syntheses of multivalent ligands coupled with effective assays that can be used to compare the contributions of different binding parameters may afford ligands that function by specific mechanisms.

L10 ANSWER 4 OF 12 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2002:155493 BIOSIS
DOCUMENT NUMBER: PREV200200155493
TITLE: Tuning cellular responses with synthetic, multivalent ligands.
AUTHOR(S): Kiessling, Laura L. [Reprint author]
CORPORATE SOURCE: Departments of Chemistry and Biochemistry, University of Wisconsin, 1101 University Avenue, Madison, WI, 53706, USA
SOURCE: Molecular Biology of the Cell, (Dec., 2000) Vol. 11, No. Supplement, pp. 426a. print.
Meeting Info.: 40th American Society for Cell Biology Annual Meeting. San Francisco, CA, USA. December 09-13, 2000. American Society for Cell Biology.
CODEN: MBCEEV. ISSN: 1059-1524.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Feb 2002
Last Updated on STN: 26 Feb 2002

L10 ANSWER 5 OF 12 EMBASE
on STN
ACCESSION NUMBER: 2003004609 EMBASE
TITLE: Influencing **receptor-ligand** binding mechanisms with **multivalent ligand** architecture.
AUTHOR: Gestwicki J.E.; Cairo C.W.; Strong L.E.; Oetjen K.A.; Kiessling L.L.
CORPORATE SOURCE: L.L. Kiessling, Department of Biochemistry, University of Wisconsin-Madison, Madison, WI 53706, United States. kiessling@chem.wisc.edu
SOURCE: Journal of the American Chemical Society, (18 Dec 2002) 124/50 (14922-14933).
Refs: 98
ISSN: 0002-7863 CODEN: JACSAT
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Multivalent ligands can function as inhibitors or effectors of biological processes. Potent inhibitory activity can arise from the high functional affinities of **multivalent ligand-receptor** interactions. Effector functions, however, are influenced not only by apparent affinities but also by alternate factors, including the ability of a **ligand** to cluster receptors. Little is known about the molecular features of a **multivalent ligand** that determine whether it will function as an inhibitor or effector. We envisioned that, by altering **multivalent ligand** architecture, ligands with preferences for different binding mechanisms would be generated. To this end, a series of 28 ligands possessing structural diversity was synthesized. This series provides the means to explore the effects of **ligand** architecture on the inhibition and clustering of a model protein, the lectin concanavalin A (Con A). The structural parameters that were varied include **scaffold** shape, size, valency, and density of binding elements. We found that ligands with certain architectures are effective inhibitors, but others mediate **receptor** clustering. Specifically, high molecular weight, polydisperse polyvalent ligands are effective inhibitors of Con A binding, whereas linear oligomeric ligands generated by the ring-opening metathesis polymerization have structural properties that favor clustering. The shape of a **multivalent ligand** also influences specific aspects of **receptor** clustering. These include the rate at which the **receptor** is clustered, the number of receptors in the

clusters, and the average interreceptor distance. Our results indicate that the architecture of a **multivalent ligand** is a key parameter in determining its activity as an inhibitor or effector. Diversity-oriented syntheses of multivalent ligands coupled with effective assays that can be used to compare the contributions of different binding parameters may afford ligands that function by specific mechanisms.

L10 ANSWER 6 OF 12 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2003:38156 SCISEARCH
THE GENUINE ARTICLE: 625LB
TITLE: Influencing **receptor-ligand** binding mechanisms with **multivalent ligand** architecture
AUTHOR: Gestwicki J E; Cairo C W; Strong L E; Oetjen K A; Kiessling L L (Reprint)
CORPORATE SOURCE: Univ Wisconsin, Dept Biochem, Madison, WI 53706 USA (Reprint); Univ Wisconsin, Dept Chem, Madison, WI 53706 USA
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, (18 DEC 2002) Vol. 124, No. 50, pp. 14922-14933.
Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA.
ISSN: 0002-7863.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 98

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Multivalent ligands can function as inhibitors or effectors of biological processes. Potent inhibitory activity can arise from the high functional affinities of **multivalent ligand-receptor** interactions. Effector functions, however, are influenced not only by apparent affinities but also by alternate factors, including the ability of a **ligand** to cluster receptors. Little is known about the molecular features of a **multivalent ligand** that determine whether it will function as an inhibitor or effector. We envisioned that, by altering **multivalent ligand** architecture, ligands with preferences for different binding mechanisms would be generated. To this end, a series of 28 ligands possessing structural diversity was synthesized. This series provides the means to explore the effects of **ligand** architecture on the inhibition and clustering of a model protein, the lectin concanavalin A (Con A). The structural parameters that were varied include **scaffold** shape, size, valency, and density of binding elements. We found that ligands with certain architectures are effective inhibitors, but others mediate **receptor** clustering. Specifically, high molecular weight, polydisperse polyvalent ligands are effective inhibitors of Con A binding, whereas linear oligomeric ligands generated by the ring-opening metathesis polymerization have structural properties that favor clustering. The shape of a **multivalent ligand** also influences specific aspects of **receptor** clustering. These include the rate at which the **receptor** is clustered, the number of receptors in the clusters, and the average interreceptor distance. Our results indicate that the architecture of a **multivalent ligand** is a key parameter in determining its activity as an inhibitor or effector. Diversity-oriented syntheses of multivalent ligands coupled with effective assays that can be used to compare the contributions of different binding parameters may afford ligands that function by specific mechanisms.

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(FILE 'HOME' ENTERED AT 16:52:08 ON 18 MAY 2004)

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     16:53:00 ON 18 MAY 2004
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L1            54 S E3
L2            44 DUP REM L1 (10 DUPLICATES REMOVED)
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                E KIESSLING/AU
                E KIESSLING L/AU
L3             0 S E6 39 E10 E11
L4           493 S E6 OR  E9 OR E10 OR E11
L5           284 DUP REM L4 (209 DUPLICATES REMOVED)
L6            53 S L5 AND LIGAND
L7       2917765 S RECEPTOR
L8        270426 S L7 AND LIGAND
L9           271 S L8 AND MULTIVALENT(A)LIGAND
L10           12 S L9 AND (SCAFFOLD OR ARRAY)
L11            6 DUP REM L10 (6 DUPLICATES REMOVED)

=> s l8 and (formylated(a)peptide)
L12           11 L8 AND (FORMYLATED(A) PEPTIDE)

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L13            6 DUP REM L12 (5 DUPLICATES REMOVED)

=> s l13 or l11
L14           12 L13 OR L11

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L13  ANSWER 1 OF 6  WPIDS  COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER:     2001-648402 [74]   WPIDS
DOC. NO. NON-CPI:     N2001-484491
DOC. NO. CPI:         C2001-191334
TITLE:                Multivalent ligands, useful for creating scaffolds of
                      biological species, including antigens, epitopes,
                      ligand binding groups, cell receptors and
                      macromolecules.
DERWENT CLASS:        B04 B05 S03
INVENTOR(S):          GESTWICKI, J E; KIESSLING, L L; STRONG, L E
PATENT ASSIGNEE(S):   (WISC) WISCONSIN ALUMNI RES FOUND
COUNTRY COUNT:        95
PATENT INFORMATION:

     PATENT NO        KIND DATE     WEEK      LA   PG
     ---------------------------------------------
     WO 2001071309    A2 20010927 (200174)* EN   95
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
            NL OA PT SD SE SL SZ TR TZ UG ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
            DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
            LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
            SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
     AU 2001081499    A  20011003 (200210)
     US 2003125262    A1 20030703 (200345)
     EP 1334118       A2 20030813 (200355)  EN
         R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
            RO SE SI TR
     JP 2004512258    W  20040422 (200428)      163

APPLICATION DETAILS:
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PATENT NO	KIND	APPLICATION	DATE
WO 2001071309	A2	WO 2001-US9174	20010321
AU 2001081499	A	AU 2001-81499	20010321
US 2003125262	A1 Provisional	US 2000-191014P	20000321
		US 2001-815296	20010321
EP 1334118	A2	EP 2001-959934	20010321
		WO 2001-US9174	20010321
JP 2004512258	W	JP 2001-569247	20010321
		WO 2001-US9174	20010321

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001081499	A Based on	WO 2001071309
EP 1334118	A2 Based on	WO 2001071309
JP 2004512258	W Based on	WO 2001071309

PRIORITY APPLN. INFO: US 2000-191014P 20000321; US 2001-815296 20010321

AN 2001-648402 [74] WPIDS

AB WO 200171309 A UPAB: 20011217

NOVELTY - A method for inducing a biological response in a biological system comprising receptors is new.

DETAILED DESCRIPTION - A method for inducing a biological response in a biological system comprising receptors comprises introduction of a multivalent **ligand** comprising signal recognition elements recognized by the receptors and bonded to a molecular scaffold.

INDEPENDENT CLAIMS are included for:

(i) a method for treating a bacterial infection comprising administration of a multivalent **ligand** comprising signal recognition elements that are chemoattractant signals covalently bonded to a molecular scaffold;

(ii) a composition for treating a bacterial infection comprising a **ligand** effective for inhibiting the chemotaxis response in the bacterium;

(iii) a method for modulating the chemotaxis response of a eukaryotic cell comprising administration of a multivalent **ligand** comprising elements that are chemoattractants of the eukaryotic cell;

(iv) a method for treating an infection of a eukaryotic pathogen or parasite comprising administration of a multivalent **ligand**;

(v) a composition for treating an infection of a eukaryotic pathogen or parasite;

(vi) a multivalent **ligand** of structure (I);

(vii) a complex of (I) bound to proteins;

(viii) a method for enhancing aggregation of biological particles comprising contacting the particles with a multivalent **ligand** comprising recognition elements which induce aggregation; and

(ix) a method for inducing apoptosis in a cell comprising administration of a multivalent **ligand** comprising signal recognition elements which bind to the cell and induce apoptosis. (I)

n = greater than 1;

Y' = O, S, NR8 or CH2;

R8 = H or organic group;

R1, R2 = H, organic group, signal recognition element (-L1-SRE), a recognition element (-L2-RE) or a functional element (-L3-FE) provided that at least one is -L1-SRE;

L1, L2, L3 = linker group; and

R4, R5, R6, R7 = H, organic group or end group.

USE - The multivalent ligands are useful for binding to any biological particle or molecules and for targeting cell or viruses. The ligands are useful for creating scaffolds of biological species, including

antigens, epitopes, **ligand** binding groups, cell receptors and macromolecules.
Dwg.0/12

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=> d his

     (FILE 'HOME' ENTERED AT 16:52:08 ON 18 MAY 2004)

     FILE 'MEDLINE, BIOSIS, EMBASE, SCISEARCH, CAPLUS, WPIDS' ENTERED AT
     16:53:00 ON 18 MAY 2004
                E KIESSLING
L1             54 S E3
L2             44 DUP REM L1 (10 DUPLICATES REMOVED)
                E AU=KIESSLING
                E KIESSLING/AU
                E KIESSLING L/AU
L3              0 S E6 39 E10 E11
L4            493 S E6 OR  E9 OR E10 OR E11
L5            284 DUP REM L4 (209 DUPLICATES REMOVED)
L6             53 S L5 AND LIGAND
L7        2917765 S RECEPTOR
L8         270426 S L7 AND LIGAND
L9            271 S L8 AND MULTIVALENT(A)LIGAND
L10            12 S L9 AND (SCAFFOLD OR ARRAY)
L11             6 DUP REM L10 (6 DUPLICATES REMOVED)
L12            11 S L8 AND (FORMYLATED(A)PEPTIDE)
L13             6 DUP REM L12 (5 DUPLICATES REMOVED)
L14            12 S L13 OR L11

=> s l9 and (cluster or clustering or clustered)
L15           43 L9 AND (CLUSTER OR CLUSTERING OR CLUSTERED)

=> dup rem l15
PROCESSING COMPLETED FOR L15
L16            15 DUP REM L15 (28 DUPLICATES REMOVED)

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L16  ANSWER 1 OF 15     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:   2004237697     IN-PROCESS
DOCUMENT NUMBER:    PubMed ID: 15136047
TITLE:              Sensor Domain of the Mycobacterium tuberculosis
                    Receptor Ser/Thr Protein Kinase, PknD, forms a
                    Highly Symmetric beta Propeller.
AUTHOR:             Good Matthew C; Greenstein Andrew E; Young Tracy A; Ng
                    Ho-Leung; Alber Tom
CORPORATE SOURCE:   Department of Molecular and Cell Biology, University of
                    California, 339 Hildebrand Hall #3206, Berkeley, CA
                    94720-3206, USA.
SOURCE:             Journal of molecular biology, (2004 May 28) 339 (2) 459-69.
                    Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY:       England: United Kingdom
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE:         Entered STN: 20040512
                    Last Updated on STN: 20040512
AB   Diverse pathogenic bacteria produce transmembrane receptor
     Ser/Thr protein kinases (STPKs), but little is known about the signals
     mediated by these "eukaryotic-like" proteins.  To explore the basis for
     signaling in the bacterial STPK receptor family, we determined
     the structure of the sensor domain of Mycobacterium tuberculosis PknD.  In
```

two crystal forms, the PknD sensor domain forms a rigid, six-bladed beta-propeller with a flexible tether to the transmembrane domain. The PknD sensor domain is the most symmetric beta-propeller structure described. All residues that vary most among the blade subdomains **cluster** in the large "cup" motif, analogous to the **ligand** -binding surface in many beta-propeller proteins. These results suggest that PknD binds a **multivalent ligand** that signals by changing the quaternary structure of the intracellular kinase domain.

=> d ibib abs l16 2-15

L16 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:256450 CAPLUS
DOCUMENT NUMBER: 138:364473
TITLE: Promoting **receptor clustering** with multivalent ligands and identifying ligands for the beta-amyloid peptide
AUTHOR(S): Cairo, Christopher Warren
CORPORATE SOURCE: Univ. of Wisconsin, Madison, WI, USA
SOURCE: (2002) 281 pp. Avail.: UMI, Order No. DA3060473 From: Diss. Abstr. Int., B 2003, 63(7), 3277
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

L16 ANSWER 3 OF 15 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2002713567 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12475334
TITLE: Influencing **receptor-ligand** binding mechanisms with **multivalent ligand** architecture.
AUTHOR: Gestwicki Jason E; Cairo Christopher W; Strong Laura E; Oetjen Karolyn A; Kiessling Laura L
CORPORATE SOURCE: Departments of Biochemistry and Chemistry, University of Wisconsin-Madison, Madison, WI 53706, USA.
CONTRACT NUMBER: GM 08349 (NIGMS)
GM 18750 (NIGMS)
GM 49975 (NIGMS)
SOURCE: Journal of the American Chemical Society, (2002 Dec 18) 124 (50) 14922-33.
Journal code: 7503056. ISSN: 0002-7863.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20021217
Last Updated on STN: 20030308
Entered Medline: 20030307
AB Multivalent ligands can function as inhibitors or effectors of biological processes. Potent inhibitory activity can arise from the high functional affinities of **multivalent ligand-receptor** interactions. Effector functions, however, are influenced not only by apparent affinities but also by alternate factors, including the ability of a **ligand** to **cluster** receptors. Little is known about the molecular features of a **multivalent ligand** that determine whether it will function as an inhibitor or effector. We envisioned that, by altering **multivalent ligand** architecture, ligands with preferences for different binding mechanisms would be generated. To this end, a series of 28 ligands possessing structural diversity was synthesized. This series provides the means to explore the effects of **ligand** architecture on the inhibition and

clustering of a model protein, the lectin concanavalin A (Con A). The structural parameters that were varied include scaffold shape, size, valency, and density of binding elements. We found that ligands with certain architectures are effective inhibitors, but others mediate **receptor clustering**. Specifically, high molecular weight, polydisperse polyvalent ligands are effective inhibitors of Con A binding, whereas linear oligomeric ligands generated by the ring-opening metathesis polymerization have structural properties that favor **clustering**. The shape of a **multivalent ligand** also influences specific aspects of **receptor clustering** . These include the rate at which the **receptor** is **clustered**, the number of receptors in the clusters, and the average interreceptor distance. Our results indicate that the architecture of a **multivalent ligand** is a key parameter in determining its activity as an inhibitor or effector. Diversity-oriented syntheses of multivalent ligands coupled with effective assays that can be used to compare the contributions of different binding parameters may afford ligands that function by specific mechanisms.

L16 ANSWER 4 OF 15 MEDLINE on STN DUPLICATE 3

ACCESSION NUMBER: 2002153140 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11853434
TITLE: Control of multivalent interactions by binding epitope density.
AUTHOR: Cairo Christopher W; Gestwicki Jason E; Kanai Motomu; Kiessling Laura L
CORPORATE SOURCE: Department of Chemistry, University of Wisconsin-Madison, Madison, Wisconsin 53706, USA.
CONTRACT NUMBER: GM08349 (NIGMS)
GM55984 (NIGMS)
SOURCE: Journal of the American Chemical Society, (2002 Feb 27) 124 (8) 1615-9.
Journal code: 7503056. ISSN: 0002-7863.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020312
Last Updated on STN: 20020511
Entered Medline: 20020510

AB **Receptor clustering** by multivalent ligands can activate signaling pathways. In principle, **multivalent ligand** features can control **clustering** and the downstream signals that result, but the influence of **ligand** structure on these processes is incompletely understood. Using a series of synthetic polymers that vary systematically, we studied the influence of **multivalent ligand** binding epitope density on the **clustering** of a model **receptor**, concanavalin A (Con A). We analyze three aspects of **receptor clustering**: the stoichiometry of the complex, rate of **cluster** formation, and **receptor** proximity. Our experiments reveal that the density of binding sites on a **multivalent ligand** strongly influences each of these parameters. In general, high binding epitope density results in greater numbers of receptors bound per polymer, faster rates of **clustering**, and reduced inter-**receptor** distances. Ligands with low binding epitope density, however, are the most efficient on a binding epitope basis. Our results provide insight into the design of ligands for controlling **receptor**-**receptor** interactions and can be used to illuminate mechanisms by which natural multivalent displays function.

L16 ANSWER 5 OF 15 MEDLINE on STN DUPLICATE 4

ACCESSION NUMBER: 2002663545 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12423961
TITLE: Synthesis of a multivalent display of a CD22-binding trisaccharide.
AUTHOR: Yang Zhi-Qiang; Puffer Erik B; Pontrello Jason K; Kiessling Laura L
CORPORATE SOURCE: Department of Chemistry, University of Wisconsin-Madison, Madison, WI 53706, USA.
CONTRACT NUMBER: GM49975 (NIGMS)
RR08389 (NCRR)
SOURCE: Carbohydrate research, (2002 Oct 8) 337 (18) 1605-13. Journal code: 0043535. ISSN: 0008-6215.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 20021109
Last Updated on STN: 20030423
Entered Medline: 20030422

AB Multivalent interactions have been implicated in the binding of B-cell surface glycoprotein CD22 to its physiological ligands. Because CD22 can influence B-cell antigen **receptor** (BCR) signaling, multivalent ligands that **cluster** CD22 may influence B-cell responses. Here, we report an efficient synthesis of a fluorophore-labeled multivalent display of a CD22-binding trisaccharide, Neu5Acalpha2,6Galbeta1,4Glc, using the ring-opening metathesis polymerization (ROMP). Our synthetic strategy involves the modification of an N-hydroxysuccinimide (NHS) ester-substituted polymer generated by ROMP with the aminopropyl glycoside of the trisaccharide. The conjugation efficiency for the coupling is high; when 0.3 equiv of the trisaccharide derivative were used relative to NHS ester groups, the mole fraction (chi) of trisaccharide **ligand** incorporated onto the backbone was 0.3. A fluorescein-labeled version of the **multivalent ligand** binds to cells expressing CD22.

L16 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:614409 CAPLUS
TITLE: Chemical approaches to eliciting and inhibiting immune responses
AUTHOR(S): Kiessling, Laura L.
CORPORATE SOURCE: Departments of Chemistry and Biochemistry, University of Wisconsin, Madison, WI, 53706, USA
SOURCE: Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002 (2002), CARB-080. American Chemical Society: Washington, D. C.
CODEN: 69CZPZ
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB To promote selective immune responses to carbohydrate epitopes, multivalent carbohydrate ligands that can bind and **cluster** the B cell antigen **receptor** (BCR) are typically used. By **clustering** the BCR, ligands can elicit signals that lead to the promotion of antibody production (i.e., function as a vaccine) or inhibition of antibody production (i.e., function as a selective immunosuppressant). The output response depends on many factors including the structure and the valency of the **multivalent ligand.** We have begun to synthesize multivalent ligands with differing structural features to examine how **ligand** structure influences the output responses of B cells. Our long-term objective is to identify ligands that selectively promote or inhibit the production of specific antibodies. Our initial results directed toward this goal will be discussed.

L16 ANSWER 7 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:101280 BIOSIS
DOCUMENT NUMBER: PREV200300101280
TITLE: The chemistry and biology of multivalent saccharide displays.
AUTHOR(S): Mann, David A. [Reprint Author]; Kiessling, Laura L. [Reprint Author]
CORPORATE SOURCE: University of Wisconsin-Madison, Madison, WI, USA
SOURCE: Wang, Peng George [Editor, Reprint Author]; Bertozzi, Carolyn R. [Editor]. (2001) pp. 221-275. Glycochemistry: Principles, synthesis, and applications. print.
Publisher: Marcel Dekker AG, Hutgasse 4, CH-4001, Postfach 812, Basel, Switzerland; Marcel Dekker Inc., 270 Madison Avenue, New York, NY, 10016, USA.
ISBN: 0-8247-0538-6 (cloth).
DOCUMENT TYPE: Book; (Book Chapter)
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Feb 2003
Last Updated on STN: 4 Apr 2003

L16 ANSWER 8 OF 15 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2000501517 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11048949
TITLE: Tuning chemotactic responses with synthetic multivalent ligands.
AUTHOR: Gestwicki J E; Strong L E; Kiessling L L
CORPORATE SOURCE: Department of Chemistry, University of Wisconsin-Madison, 53706, USA.
CONTRACT NUMBER: GM 18750 (NIGMS)
GM 55984 (NIGMS)
T32GM08349 (NIGMS)
SOURCE: Chemistry & biology, (2000 Aug) 7 (8) 583-91.
Journal code: 9500160. ISSN: 1074-5521.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010202

AB BACKGROUND: Multivalent ligands have been used previously to investigate the role of **ligand** valency and **receptor clustering** in eliciting biological responses. Studies of **multivalent ligand** function, however, typically have employed divalent ligands or ligands of undefined valency. How cells respond to multivalent ligands of distinct valencies, which can **cluster** a signaling **receptor** to different extents, has never been examined. The chemoreceptors, which mediate chemotactic responses in bacteria, are localized, and **clustering** has been proposed to play a role in their function. Using multivalent ligands directed at the chemoreceptors, we hypothesized that we could exploit **ligand** valency to control **receptor** occupation and **clustering** and, ultimately, the cellular response. RESULTS: To investigate the effects of **ligand** valency on the bacterial chemotactic response, we generated a series of linear multivalent arrays with distinct valencies by ring-opening metathesis polymerization. We report that these synthetic ligands elicit bacterial chemotaxis in both Escherichia coli and Bacillus subtilis. The chemotactic response depended on the valency of the **ligand**; the response of the bacteria can be altered by varying chemoattractant **ligand** valency. Significantly, these differences in chemotactic responses were related to the ability of the multivalent ligands to **cluster** chemoreceptors

at the plasma membrane. CONCLUSIONS: Our results demonstrate that **ligand** valency can be used to tune the chemotactic responses of bacteria. This mode of regulation may arise from changes in **receptor** occupation or changes in **receptor clustering** or both. Our data implicate changes in **receptor clustering** as one important mechanism for altering cellular responses. Given the diverse events modulated by changes in the spatial proximity of cell surface receptors, our results suggest a general strategy for tuning biological responses.

L16 ANSWER 9 OF 15 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 97213450 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9060179
TITLE: Effect of dimerization of the D-glucose analogue of muramyl dipeptide on stimulation of macrophage-like cells.
AUTHOR: Murata J; Kitamoto T; Ohya Y; Ouchi T
CORPORATE SOURCE: Department of Applied Chemistry, Faculty of Engineering, Kansai University, Osaka, Japan.
SOURCE: Carbohydrate research, (1997 Jan 2) 297 (2) 127-33.
Journal code: 0043535. ISSN: 0008-6215.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970507
Last Updated on STN: 19970507
Entered Medline: 19970429

AB N-Acetylmuramyl-L-alanyl-D-isoglutamine (MDP) is the minimum required structure responsible for the immunoadjuvant activity of the bacterial cell wall. The D-glucose analogue of MDP (GADP) was reported to show a higher immunoadjuvant activity than MDP itself. Although the mechanism of activation by MDP and the existence of **receptor** against MDP are not clear, the patch formation and **cluster** formation of receptors are important steps on the signal transduction by such bioactive molecules. It is expected that the **cluster** effect such as antennary oligosaccharides reported by Lee et al. increased the affinity of **ligand** against **receptor** and accelerated the patch formation and **cluster** formation of receptors. In order to discuss the effect of **multivalent-ligand** formation of GADP on the activation of immunocompetent cells in more detail, we have synthesized GADP dimers combined through various lengths of alkyl and poly(ethylene glycol) (PEG) spacer groups as the simple models of **multivalent-ligand** molecule of GADP and evaluated their immunological enhancement activities in vitro. The GADP dimers showed a higher level stimulatory activities against macrophage-like cells than free GADP and monomeric GADP derivatives.

L16 ANSWER 10 OF 15 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 94347757 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7520751
TITLE: **Multivalent ligand-receptor** binding interactions in the fibroblast growth factor system produce a cooperative growth factor and heparin mechanism for **receptor** dimerization.
AUTHOR: Pantoliano M W; Horlick R A; Springer B A; Van Dyk D E; Tobery T; Wetmore D R; Lear J D; Nahapetian A T; Bradley J D; Sisk W P
CORPORATE SOURCE: Crystallography and Biophysical Chemistry Group, Du Pont Merck Pharmaceutical Company, Wilmington, Delaware 19880.
SOURCE: Biochemistry, (1994 Aug 30) 33 (34) 10229-48.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199409
ENTRY DATE: Entered STN: 19941006
Last Updated on STN: 19960129
Entered Medline: 19940927

AB The binding interactions for the three primary reactants of the fibroblast growth factor (FGF) system, basic FGF (bFGF), an FGF **receptor**, FGFR1, and the cofactor heparin/heparan sulfate (HS), were explored by isothermal titrating calorimetry, ultracentrifugation, and molecular modeling. The binding reactions were first dissected into three binary reactions: (1) FGFR1 + bFGF<==>FGFR1/bFGF, K1 = 41 (+/- 12) nM; (2) FGFR1 + HS<==>FGFR1/HS, K2 = 104 (+/- 17) microM; and (3) bFGF + HS<==>bFGF/HS, K3 = 470 (+/- 20) nM, where HS = low MW heparin, approximately 3 kDa. The first, binding of bFGF to FGFR1 in the absence of HS, was found to be a simple binary binding reaction that is enthalpy dominated and characterized by a single equilibrium constant, K1. The conditional reactions of bFGF and FGFR1 in the presence of heparin were then examined under conditions that saturate only the bFGF heparin site (1.5 equiv of HS/bFGF) or saturate the HS binding sites of both bFGF and FGFR1 (1.0 mM HS). Both 3-and 5-kDa low MW heparins increased the affinity for FGFR1 binding to bFGF by approximately 10-fold (Kd = 4.9 +/- 2.0 nM), relative to the reaction with no HS. In addition, HS, at a minimum of 1.5 equiv/bFGF, induced a second FGFR1 molecule to bind to another lower affinity secondary site on bFGF (K4 = 1.9 +/- 0.7 microM) in an entropy-dominated reaction to yield a quaternary complex containing two FGFR1, one bFGF, and at least one HS. Molecular weight estimates by analytical ultracentrifugation of such fully bound complexes were consistent with this proposed composition. To understand these binding reactions in terms of structural components of FGFR1, a three-dimensional model of FGFR1 was constructed using segment match modeling. Electrostatic potential calculations confirmed that an elongated **cluster**, approximately 15 x 35 A, of nine cationic residues focused positive potential (+2kBT) to the solvent-exposed beta-sheet A, B, E, C' surface of the D(II) domain model, strongly implicating this locus as the HS binding region of FGFR1. Structural models for HS binding to FGFR1, and HS binding to bFGF, were built individually and then assembled to juxtapose adjacent binding sites for **receptor** and HS on bFGF, against matching proposed growth factor and HS binding sites on FGFR1. The calorimetric binding results and the molecular modeling exercises suggest that bFGF and HS participate in a concerted bridge mechanism for the dimerization of FGFR1 in vitro and presumably for mitogenic signal transduction in vivo.(ABSTRACT TRUNCATED AT 400 WORDS)

L16 ANSWER 11 OF 15 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 92:642158 SCISEARCH
THE GENUINE ARTICLE: JV613
TITLE: **MULTIVALENT LIGAND**-BINDING BY SERUM MANNOSE-BINDING PROTEIN
AUTHOR: LEE R T (Reprint); ICHIKAWA Y; KAWASAKI T; DRICKAMER K; LEE Y C
CORPORATE SOURCE: JOHNS HOPKINS UNIV, DEPT BIOL, BALTIMORE, MD, 21218 (Reprint); JOHNS HOPKINS UNIV, MCCOLLUM PRATT INST, BALTIMORE, MD, 21218; KYOTO UNIV, FAC PHARMACEUT SCI, DEPT BIOL CHEM, KYOTO 606, JAPAN; COLUMBIA UNIV, DEPT BIOCHEM & MOLEC BIOPHYS, NEW YORK, NY, 10032
COUNTRY OF AUTHOR: USA; JAPAN
SOURCE: ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, (15 NOV 1992) Vol. 299, No. 1, pp. 129-136.
ISSN: 0003-9861.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE

LANGUAGE: ENGLISH
REFERENCE COUNT: 41

L16 ANSWER 12 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1982:279166 BIOSIS
DOCUMENT NUMBER: PREV198274051646; BA74:51646
TITLE: MEMBER ASSOCIATED CHANGES DURING ERYTHROPOIESIS MECHANISM OF MATURATION OF RETICULOCYTES TO ERYTHROCYTES.
AUTHOR(S): ZWEIG S E [Reprint author]; TOKYUASU K T; SINGER S J
CORPORATE SOURCE: LAB IMMUNOL, NATIONAL INST ALLERGY INFECTIOUS DISEASES, NATIONAL INST HEALTH, BETHESDA, MD 20205, USA
SOURCE: Journal of Supramolecular Structure and Cellular Biochemistry, (1981) Vol. 17, No. 2, pp. 163-182.
CODEN: JSSBDH. ISSN: 0275-3723.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB The mature mammalian erythrocyte has a unique membranoskeleton, the spectrin-actin complex, which is responsible for many of the unusual membrane properties of the erythrocyte. In successive stages of differentiation of the erythropoietic series leading to the mature erythrocyte there is a progressive increase in the density of spectrin associated with the membranes of these cells. An important stage of this progression occurs during the enucleation of the late erythroblast to produce the incipient reticulocyte, when all of the spectrin of the former cell is sequestered to the membrane of the reticulocyte. The reticulocyte does not exhibit a fully formed membranoskeleton. The in vitro binding of multivalent ligands to specific membrane receptors on the reticulocyte caused a **clustering** of some fractions of these **ligand-receptor** complexes into special mobile domains on the cell surface. These domains of **clustered ligand-receptor** complexes became invaginated and endocytosed as small vesicles. By immuno-electron microscopic experiments, these invaginations and endocytosed vesicles were specifically free of spectrin on their cytoplasmic surfaces. The maturation of reticulocytes to mature erythrocytes in vivo might involve a progressive loss of reticulocyte membrane free of spectrin, thereby producing a still more concentrated spectrin-actin membranoskeleton in the erythrocyte than in the reticulocyte. In vivo reticulocytes were observed in ultrathin frozen sections of spleens from rabbits rendered anemic by phenylhydrazine treatment. These sections were indirectly immunolabeled with ferritin-antibody reagents directed to rabbit spectrin. Most reticulocytes in a section had 1 or more surface invaginations and 1 or more intracellular vesicles that were devoid of spectrin labeling. The erythrocytes in the same sections did not exhibit these features, and their membranes were uniformly labeled for spectrin. Spectrin-free surface invaginations and intracellular vesicle were also observed with reticulocytes within normal rabbit spleens. A scheme for membrane remodeling during reticulocyte maturation in vivo is proposed.

L16 ANSWER 13 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 8
ACCESSION NUMBER: 1981:216286 BIOSIS
DOCUMENT NUMBER: PREV198172001270; BA72:1270
TITLE: **RECEPTOR CLUSTERING** ON A CELL SURFACE
3. THEORY OF **RECEPTOR** CROSS LINKING BY MULTIVALENT LIGANDS DESCRIPTION BY **LIGAND** STATES.
AUTHOR(S): PERELSON A S [Reprint author]
CORPORATE SOURCE: DIV BIOL MED, LEFSCHETZ CENT DYNAMICAL SYST, BROWN UNIV, PROVIDENCE, RI 02912, USA
SOURCE: Mathematical Biosciences, (1981) Vol. 53, No. 1-2, pp. 1-40.
CODEN: MABIAR. ISSN: 0025-5564.

DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB The interaction of **multivalent ligand** with cell surface receptors is the 1st-step in triggering a number of biological responses. A mathematical model for the binding of a **multivalent ligand**, containing v identical reactive sites, to monovalent or multivalent cell surface receptors is presented and analyzed. The initial binding of such ligands to a cell is followed by further reactions on the surface which cross-link receptors and lead to the formation of **ligand-receptor** clusters. In the presence of monovalent haptens the possibility that **clustering** can be competitively inhibited is considered. By introducing the concept of an effective valence for the **ligand**, which is the number of reactive groups that can simultaneously bind to surface receptors, one can take into account steric hindrance and the inability of some **ligand** determinants to participate in cross-linking reactions because they are oriented incorrectly. When the **ligand**'s effective valence is > 2, a number of different criteria can be used to measure **receptor clustering**: the fraction of **receptor** sites occupied by multiply bound **ligand**, the concentration of cross-links holding distinct receptors together and the concentration of cell surface aggregates. The dependence of these 3 aggregation measures on **ligand** and monovalent hapten concentration is studied. A number of theorems are proven about the general shape and characteristics of cross-linking curves. For ligands which can simultaneously bind > 2 cell surface receptors the cross-linking curve is not symmetric, although as in the case of bivalent ligands, the curve generated using the first 2 criteria has a single maximum. Throughout the analysis intramolecular reactions and ring formation are ignored. A criterion is developed which indicates that the theory can break down at high degrees of cross-linking for receptors which have 2 or more combining sites. In such cases intramolecular reactions need to be considered. As an application, the theory is used to interpret previously published experiments on the release of histamine by basophils.

L16 ANSWER 14 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 9

ACCESSION NUMBER: 1981:195734 BIOSIS
DOCUMENT NUMBER: PREV198171065726; BA71:65726
TITLE: THEORY OF **CLUSTERING** OF CELL SURFACE RECEPTORS BY LIGANDS OF ARBITRARY VALENCE DEPENDENCE OF DOSE RESPONSE PATTERNS ON A COARSE **CLUSTER** CHARACTERISTIC.
AUTHOR(S): DELISI C [Reprint author]
CORPORATE SOURCE: LAB THEORETICAL BIOL, NATIONAL CANCER INST, NATIONAL INST HEALTH, BETHESDA, MD 20205, USA
SOURCE: Mathematical Biosciences, (1980) Vol. 52, No. 3-4, pp. 159-184.
CODEN: MABIAR. ISSN: 0025-5564.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB The interaction of ligands with cell surface receptors often induces the formation of **receptor** clusters on the plasma membrane as in fibroblast mitogenesis induced by epidermal growth factor and insulin induced glucose oxidation by adipocytes. Methods for calculating the kinetics of **clustering** of divalent receptors by ligands of arbitrary valence are developed. Intramolecular bonding (i.e., both sites on the same **receptor** bound to a single **ligand**) is explicitly included in the formalism. The equations are necessary for a quantitative analysis of the response of basophils and mast cells to multivalent haptens and antigens. The implications of the equations are briefly pursued. The presence of intramolecular reaction has 2 opposing

effects on the concentration of cross-links, increasing them at low **ligand** concentrations and suppressing them at high **ligand** concentrations. Those bivalent haptens which do not induce a response may be active when they are in the form of higher valence analogs. The relation K = 1/2c* between the **ligand** concentration at which histamine release peaks (c*) and the **ligand** site-**receptor** site affinity (K), which holds for symmetric bivalent haptens, has no simple exact analog for **multivalent ligand**. A good approximate relation that holds when .**GRAPHIC**. > Kc* is .**GRAPHIC**. = 1/fc*, where .**GRAPHIC**. is the intramolecular equilibrium constant at very low **ligand** concentrations, and f (≥ 2) is the valence of the **ligand**. The dose dependence of a response that is proportional to concentration of cross-links is qualitatively different from one that is proportional to the concentration of aggregates. In particular, the concentration of aggregates may be a bimodal function of **ligand** concentration. The deviations from simple unimodal dose-response patterns that are sometimes observed in histamine release experiments may in part reflect the cell's inability to discriminate between **cluster** sizes beyond a certain small size. The dose dependence of the number of aggregates per cell shows a switch from unimodal to bimodal as valence is increased. The bimodal pattern is markedly asymmetric, with a high concentration peak that is considerably larger than the low concentration peak. For conditions under which such bimodality is obtained, the addition of monomer will decrease of number of aggregates at very low concentrations, but increase the number over the limb that descends from the low concentration mode. For low affinity ligands (K = 104 M-1), the low concentration mode will be the only one observed. A response that is a function of the number of aggregates will sometimes be observed to increase at supraoptimal concentrations when monomer is added. The number of aggregates induced by bivalent ligands can, for certain limited but relevant concentration and parameter ranges, exceed the number induced by higher valence analogs. The predictions are discussed in terms of available experimental data.

L16 ANSWER 15 OF 15 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 81026424 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6968316
TITLE: Role of coated vesicles, microfilaments, and calmodulin in **receptor**-mediated endocytosis by cultured B lymphoblastoid cells.
AUTHOR: Salisbury J L; Condeelis J S; Satir P
CONTRACT NUMBER: GM 25813 (NIGMS)
HL 22560 (NHLBI)
SOURCE: Journal of cell biology, (1980 Oct) 87 (1) 132-41.
Journal code: 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198012
ENTRY DATE: Entered STN: 19900316
Last Updated on STN: 19970203
Entered Medline: 19801218

AB Cell surface **receptor** IgM molecules of cultured human lymlphoblastoid cells (WiL2) patch and redistribute into a cap over the Golgi region of the cell after treatment with multivalent anti-IgM antibodies. During and after the redistribution, **ligand**-**receptor** clusters are endocytosed into coated pits and coated vesicles. Morphometric analysis of the distribution of ferritin-labeled **ligand** at EM resolution reveals the following sequence of events in the endocytosis of cell surface IgM: (a) binding of the **multivalent ligand** in a diffuse cell surface distribution, (b) **clustering** of the **ligand**-

receptor complexes, (c) recruitment of clathrin coats to the cytoplasmic surface of the cell membrane opposite **ligand-receptor** clusters, (d) assembly and (e) internalization of coated vesicles, and (f) delivery of label into a large vesicular compartment, presumably partly lysosomal. Most of the labeled **ligand** enters this pathway. The recruitment of clathrin coats to the membrane opposite **ligand-receptor** clusters is sensitive to the calmodulin-directed drug Stelazine (trifluoperazine dihydrochloride). In addition, Stelazine inhibits an alternate pathway of endocytosis that does not involve coated vesicle formation. The actin-directed drug dihydrocytochalasin B has no effect on the recruitment of clathrin to the **ligand-receptor** clusters and the formation of coated pits and little effect on the alternate pathway, but this drug does interfere with subsequent coated vesicle formation and it inhibits capping. Cortical microfilaments that decorate with heavy meromyosin with constant polarity are observed in association with the coated regions of the plasma membrane and with coated vesicles. SDS-polyacrylamide gel electrophoresis analysis of a coated vesicle preparation isolated from WiL2 cells demonstrates that the major polypeptides in the fraction are a 175-kdalton component that comigrates with calf brain clathrin, a 42-kdalton component that comigrates with rabbit muscle actin and a 18.5-kdalton minor component that comigrates with calmodulin as well as 110-, 70-, 55-, 36-, 30-, and 17-kdalton components. These results clarify the pathways of endocytosis in this cell and suggest functional roles for calmodulin, especially in the formation of clathrin-coated pits, and for actin microfilaments in coated vesicle formation and in capping.

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=> d his

     (FILE 'HOME' ENTERED AT 16:52:08 ON 18 MAY 2004)

     FILE 'MEDLINE, BIOSIS, EMBASE, SCISEARCH, CAPLUS, WPIDS' ENTERED AT
     16:53:00 ON 18 MAY 2004
                E KIESSLING
L1            54 S E3
L2            44 DUP REM L1 (10 DUPLICATES REMOVED)
                E AU=KIESSLING
                E KIESSLING/AU
                E KIESSLING L/AU
L3             0 S E6 39 E10 E11
L4           493 S E6 OR  E9 OR E10 OR E11
L5           284 DUP REM L4 (209 DUPLICATES REMOVED)
L6            53 S L5 AND LIGAND
L7       2917765 S RECEPTOR
L8        270426 S L7 AND LIGAND
L9           271 S L8 AND MULTIVALENT(A)LIGAND
L10           12 S L9 AND (SCAFFOLD OR ARRAY)
L11            6 DUP REM L10 (6 DUPLICATES REMOVED)
L12           11 S L8 AND (FORMYLATED(A)PEPTIDE)
L13            6 DUP REM L12 (5 DUPLICATES REMOVED)
L14           12 S L13 OR L11
L15           43 S L9 AND (CLUSTER OR CLUSTERING OR CLUSTERED)
L16           15 DUP REM L15 (28 DUPLICATES REMOVED)

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FULL ESTIMATED COST                                     300.84     301.26

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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	ENTRY	SESSION
CA SUBSCRIBER PRICE	-33.26	-33.26

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NEWS	3	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS	4	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS	5	FEB 05	German (DE) application and patent publication number format changes
NEWS	6	MAR 03	MEDLINE and LMEDLINE reloaded
NEWS	7	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS	8	MAR 03	FRANCEPAT now available on STN
NEWS	9	MAR 29	Pharmaceutical Substances (PS) now available on STN
NEWS	10	MAR 29	WPIFV now available on STN
NEWS	11	MAR 29	New monthly current-awareness alert (SDI) frequency in RAPRA
NEWS	12	APR 26	PROMT: New display field available
NEWS	13	APR 26	IFIPAT/IFIUDB/IFICDB: New super search and display field available
NEWS	14	APR 26	LITALERT now available on STN
NEWS	15	APR 27	NLDB: New search and display fields available
NEWS	16	May 10	PROUSDDR now available on STN
NEWS	17	May 19	PROUSDDR: One FREE connect hour, per account, in both May and June 2004
NEWS	18	May 12	EXTEND option available in structure searching
NEWS	19	May 12	Polymer links for the POLYLINK command completed in REGISTRY
NEWS	20	May 17	FRFULL now available on STN

NEWS EXPRESS	MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 17:50:58 ON 18 MAY 2004

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=> FILE MEDLINE, BIOSIS, EMBASE, SCISEARCH, CAPLUS, WPIDS
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                               0.21       0.21

FILE 'MEDLINE' ENTERED AT 17:51:26 ON 18 MAY 2004

FILE 'BIOSIS' ENTERED AT 17:51:26 ON 18 MAY 2004
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FILE 'EMBASE' ENTERED AT 17:51:26 ON 18 MAY 2004
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FILE 'SCISEARCH' ENTERED AT 17:51:26 ON 18 MAY 2004
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FILE 'CAPLUS' ENTERED AT 17:51:26 ON 18 MAY 2004
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FILE 'WPIDS' ENTERED AT 17:51:26 ON 18 MAY 2004
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=> S RECEPTOR AND LIGAND
L1      270426 RECEPTOR AND LIGAND

=> S L1 AND (FORMYLATED(A)PEPTIDE)
L2           11 L1 AND (FORMYLATED(A) PEPTIDE)

=> DUB REM
DUB IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> DUP REM
ENTER L# LIST OR (END):L2
PROCESSING COMPLETED FOR L2
L3             6 DUP REM L2 (5 DUPLICATES REMOVED)

=> D IBIB ABS L3 1-6

L3   ANSWER 1 OF 6  WPIDS  COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER:     2001-648402 [74]   WPIDS
DOC. NO. NON-CPI:     N2001-484491
DOC. NO. CPI:         C2001-191334
TITLE:                Multivalent ligands, useful for creating scaffolds of
                      biological species, including antigens, epitopes,
                      ligand binding groups, cell receptors and
                      macromolecules.
DERWENT CLASS:        B04 B05 S03
INVENTOR(S):          GESTWICKI, J E; KIESSLING, L L; STRONG, L E
PATENT ASSIGNEE(S):   (WISC) WISCONSIN ALUMNI RES FOUND
COUNTRY COUNT:        95
PATENT INFORMATION:

     PATENT NO        KIND DATE     WEEK      LA   PG
     ---------------------------------------------
     WO 2001071309    A2 20010927 (200174)* EN   95
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
            NL OA PT SD SE SL SZ TR TZ UG ZW
```

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2001081499 A 20011003 (200210)
US 2003125262 A1 20030703 (200345)
EP 1334118 A2 20030813 (200355) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI TR
JP 2004512258 W 20040422 (200428) 163

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001071309	A2	WO 2001-US9174	20010321
AU 2001081499	A	AU 2001-81499	20010321
US 2003125262	A1 Provisional	US 2000-191014P	20000321
		US 2001-815296	20010321
EP 1334118	A2	EP 2001-959934	20010321
		WO 2001-US9174	20010321
JP 2004512258	W	JP 2001-569247	20010321
		WO 2001-US9174	20010321

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001081499	A	Based on	WO 2001071309
EP 1334118	A2	Based on	WO 2001071309
JP 2004512258	W	Based on	WO 2001071309

PRIORITY APPLN. INFO: US 2000-191014P 20000321; US 2001-815296 20010321

AN 2001-648402 [74] WPIDS

AB WO 200171309 A UPAB: 20011217

NOVELTY - A method for inducing a biological response in a biological system comprising receptors is new.

DETAILED DESCRIPTION - A method for inducing a biological response in a biological system comprising receptors comprises introduction of a multivalent **ligand** comprising signal recognition elements recognized by the receptors and bonded to a molecular scaffold.

INDEPENDENT CLAIMS are included for:

(i) a method for treating a bacterial infection comprising administration of a multivalent **ligand** comprising signal recognition elements that are chemoattractant signals covalently bonded to a molecular scaffold;

(ii) a composition for treating a bacterial infection comprising a **ligand** effective for inhibiting the chemotaxis response in the bacterium;

(iii) a method for modulating the chemotaxis response of a eukaryotic cell comprising administration of a multivalent **ligand** comprising elements that are chemoattractants of the eukaryotic cell;

(iv) a method for treating an infection of a eukaryotic pathogen or parasite comprising administration of a multivalent **ligand**;

(v) a composition for treating an infection of a eukaryotic pathogen or parasite;

(vi) a multivalent **ligand** of structure (I);

(vii) a complex of (I) bound to proteins;

(viii) a method for enhancing aggregation of biological particles comprising contacting the particles with a multivalent **ligand** comprising recognition elements which induce aggregation; and

(ix) a method for inducing apoptosis in a cell comprising

administration of a multivalent **ligand** comprising signal recognition elements which bind to the cell and induce apoptosis. (I)

n = greater than 1;

Y' = O, S, NR8 or CH2;

R8 = H or organic group;

R1, R2 = H, organic group, signal recognition element (-L1-SRE), a recognition element (-L2-RE) or a functional element (-L3-FE) provided that at least one is -L1-SRE;

L1, L2, L3 = linker group; and

R4, R5, R6, R7 = H, organic group or end group.

USE - The multivalent ligands are useful for binding to any biological particle or molecules and for targeting cell or viruses. The ligands are useful for creating scaffolds of biological species, including antigens, epitopes, **ligand** binding groups, cell receptors and macromolecules.

Dwg.0/12

L3 ANSWER 2 OF 6 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2001:258526 BIOSIS

DOCUMENT NUMBER: PREV200100258526

TITLE: Nociceptin and its **receptor** are present in human peripheral blood leukocytes: A new link between pain and inflammation.

AUTHOR(S): Pouliot, Marc [Reprint author]; Gilbert, Caroline [Reprint author]

CORPORATE SOURCE: Laval University, 2705 Laurier Boulevard, Suite T1-49, Sainte-Foy, Quebec, G1V 4G2, Canada

SOURCE: FASEB Journal, (March 8, 2001) Vol. 15, No. 5, pp. A1213. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001. Orlando, Florida, USA. March 31-April 04, 2001.
CODEN: FAJOEC. ISSN: 0892-6638.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 30 May 2001
Last Updated on STN: 19 Feb 2002

AB The nociceptin **receptor** (NociR) is a GTP-binding protein-coupled **receptor** sharing sequence homology with opioid receptors and present in neural tissues. Its activation by nociceptin in the central nervous system has been linked to a range of physiological functions, including the processing of pain signals. Nociceptin can be released in the periphery from primary afferent nerve fibers and thus may act at various sites such as the skin, visceral organs and blood vessels, suggesting that additional physiological functions of this neuropeptide have yet to be appreciated. In this study, we determined whether this neuropeptide may impact on the immune system. We found that nociceptin and its **receptor**, NociR, are expressed in immune cells, including human peripheral blood leukocytes. Messenger RNA for NociR as well for the **ligand** precursor, prepronociceptin, were observed in polymorphonuclear leukocytes (PMNs), monocytes and lymphocytes. FACS analysis on total leukocyte preparations using fluorescent nociceptin as the **ligand** indicated that PMNs express the highest levels of surface-NociR among circulating leukocytes. PMNs stimulated with the synthetic **formylated peptide** f-Methionyl-Leucyl-Phenylalanine (fMLP) were found to release immunoreactive nociceptin, as measured by ELISA. On the other hand, PMNs incubated with nociceptin displayed a specific pattern of cellular protein phosphorylation on tyrosine residues, suggesting that NociR is functional in circulating leukocytes and indicating that its engagement by nociceptin may elicits selected cellular responses. These results show that the nociceptin/NociR system is active in immune cells and may represent a new link between the

nervous and the immune systems.

L3 ANSWER 3 OF 6 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:258478 BIOSIS
DOCUMENT NUMBER: PREV200100258478
TITLE: Nociceptin and its **receptor** are present in human peripheral blood leukocytes: A new link between pain and inflammation.
AUTHOR(S): Pouliot, Marc [Reprint author]; Gilbert, Caroline [Reprint author]
CORPORATE SOURCE: Laval University, 2705 Laurier Boulevard, Suite T1-49, Sainte-Foy, Quebec, G1V 4G2, Canada
SOURCE: FASEB Journal, (March 8, 2001) Vol. 15, No. 5, pp. A1167. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001. Orlando, Florida, USA. March 31-April 04, 2001.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 May 2001
Last Updated on STN: 19 Feb 2002

AB The nociceptin **receptor** (NociR) is a GTP-binding protein-coupled **receptor** sharing sequence homology with opioid receptors and present in neural tissues. Its activation by nociceptin in the central nervous system has been linked to a range of physiological functions, including the processing of pain signals. Nociceptin can be released in the periphery from primary afferent nerve fibers and thus may act at various sites such as the skin, visceral organs and blood vessels, suggesting that additional physiological functions of this neuropeptide have yet to be appreciated. In this study, we determined whether this neuropeptide may impact on the immune system. We found that nociceptin and its **receptor**, NociR, are expressed in immune cells, including human peripheral blood leukocytes. Messenger RNA for NociR as well for the **ligand** precursor, prepronociceptin, were observed in polymorphonuclear leukocytes (PMNs), monocytes and lymphocytes. FACS analysis on total leukocyte preparations using fluorescent nociceptin as the **ligand** indicated that PMNs express the highest levels of surface-NociR among circulating leukocytes. PMNs stimulated with the synthetic **formylated peptide** f-Methionyl-Leucyl-Phenylalanine (fMLP) were found to release immunoreactive nociceptin, as measured by ELISA. On the other hand, PMNs incubated with nociceptin displayed a specific pattern of cellular protein phosphorylation on tyrosine residues, suggesting that NociR is functional in circulating leukocytes and indicating that its engagement by nociceptin may elicits selected cellular responses. These results show that the nociceptin/NociR system is active in immune cells and may represent a new link between the nervous and the immune systems.

L3 ANSWER 4 OF 6 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 1998:543121 SCISEARCH
THE GENUINE ARTICLE: ZZ127
TITLE: Modulation by interferon-gamma of the production and gene expression of IL-1 **receptor** antagonist in human neutrophils
AUTHOR: McDonald P P (Reprint); Gasperini S; Calzetti F; Cassatella M A
CORPORATE SOURCE: INST GEN PATHOL, STRADA GRAZIE 4, I-37134 VERONA, ITALY (Reprint)
COUNTRY OF AUTHOR: ITALY
SOURCE: CELLULAR IMMUNOLOGY, (25 FEB 1998) Vol. 184, No. 1, pp. 45-50.

Publisher: ACADEMIC PRESS INC JNL-COMP SUBSCRIPTIONS, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495.
ISSN: 0008-8749.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 31
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In this report, we show that interferon-gamma (IFN-gamma) modulates the production of IL-1ra in activated human neutrophils. In lipopolysaccharide-stimulated cells, IFN-gamma increased the release of IL-1ra without modulating IL-1ra mRNA accumulation; under these conditions, IFN-gamma only marginally enhanced IL-1ra de novo synthesis, while IL-1ra was more efficiently secreted. In response to the **formylated peptide**, fMLP, neutrophils released small but significant amounts of IL-1ra, yet without an increase in IL-1ra mRNA over constitutive levels. Following IFN-gamma treatment, however, the fMLP elicited IL-1ra production was greatly potentiated, and this was accompanied by a transient increased accumulation of IL-1ra mRNA Finally, opsonized yeast particles were found to induce IL-1ra formation at late incubation times, and prior treatment of neutrophils with IFN-gamma moderately enhanced this response. Collectively, our results demonstrate that in neutrophils activated by different classes of agonists, IFN-gamma modulates the release of IL-1ra by acting through distinct mechanisms. (C) 1998 Academic Press.

L3 ANSWER 5 OF 6 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 88087431 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3121639
TITLE: Regulation of the affinity state of the N-**formylated peptide receptor** of neutrophils: role of guanine nucleotide-binding proteins and the cytoskeleton.
AUTHOR: Painter R G; Zahler-Bentz K; Dukes R E
CORPORATE SOURCE: Department of Biochemistry, University of Texas Health Center, Tyler 75710.
CONTRACT NUMBER: GM-35127 (NIGMS)
HL-34998 (NHLBI)
SOURCE: Journal of cell biology, (1987 Dec) 105 (6 Pt 2) 2959-71.
Journal code: 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198802
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 20021218
Entered Medline: 19880220

AB Previous studies have indicated that the **receptor** for N-formylated peptides present on human neutrophils can exist in several **ligand**-dissociation states at least one of which is sensitive to guanine nucleotides. Human neutrophil membranes rich in cell surface enzyme markers have been isolated from cells pretreated at 37 degrees C with 5 nM fluoresceinated chemotactic peptide (N-formyl-Nle-Leu-Phe-Nle-Tyr-Lys-fluorescein; Fl-peptide) or a buffer control and analyzed for **receptor**-**ligand** dissociation states using a previously published fluorescence assay for estimating **ligand** binding and dissociation rates (Sklar, L. A., et al. 1984. J. Biol. Chemical 259:5661-5669). Fractionation of crude microsomes derived from homogenates of unstimulated cells by ultracentrifugation on linear D2O gradients yielded two plasma membrane-rich fractions termed fast and slow microsomes. Analysis of Fl-peptide dissociation rates from **receptor** present in fast membrane fractions of unstimulated cells

yielded data that could be best fit by assuming that the **receptor** exists in three distinct **ligand**-dissociation states. The intermediate **ligand**-dissociation state (state B) accounted for 47% of the total and was converted to the fastest **ligand** -dissociation state (state A) by incubation of membranes with GTP or GTP-gamma-S. The remainder of the **receptor** (17%) present in unstimulated membranes was in a state from which **ligand** was virtually nondissociable (state C). This form of the **receptor** was insensitive to GTP-gamma-S. When cells were stimulated with Fl-peptide, most of the **receptor** present in slow and fast membranes was of the state C type. In contrast to unstimulated cells, slow membranes derived from cells exposed to Fl-peptide contained the majority of the recoverable **receptor** indicating that **receptor** was transferred to a physically isolatable membrane domain after **ligand** binding to the intact cell. The **ligand**-induced formation of state C in both fast and slow microsome fractions was inhibited by treatment of cells with dihydrocytochalasin B. However, the drug had no effect on translocation of the **receptor** to slow membranes. Pertussis toxin treatment of intact cells had no effect on **ligand**-induced formation of state C in either fraction even though other cellular responses were inhibited. Both slow and fast membranes contained a 41-kD G protein as assayed by immunoblot analysis. The data suggest that **ligand** induces a segregation of **receptor-ligand** complexes into a membrane domain in which the **receptor** is functionally uncoupled from the 41-kD neutrophil G protein.(ABSTRACT TRUNCATED AT 400 WORDS)

L3 ANSWER 6 OF 6 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 84307439 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6089766
TITLE: Secretagogue-induced phosphoinositide metabolism in human leucocytes.
AUTHOR: Dougherty R W; Godfrey P P; Hoyle P C; Putney J W Jr; Freer R J
CONTRACT NUMBER: DE-05764 (NIDCR)
SOURCE: Biochemical journal, (1984 Sep 1) 222 (2) 307-14.
Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198410
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 20000303
Entered Medline: 19841024

AB The relationship between **receptor** binding of the **formylated peptide** chemoattractant formylmethionylleucylphenylalanine (fMet-Leu-Phe), lysosomal enzyme secretion and metabolism of membrane phospholipids was evaluated in both human polymorphonuclear leucocytes (PMN) and the dimethyl sulphoxide (Me2SO)-stimulated human myelomonocytic HL-60 leukaemic cell line. In both cell types, exposure to fMet-Leu-Phe (100 nM) induced rapid lysosomal enzyme secretion (maximal release less than 30 s) and marked changes in the 32P-labelling of the inositol lipids phosphatidylinositol (PtdIns), phosphatidylinositol 4-phosphate (PtdIns4P), phosphatidylinositol 4,5-bisphosphate [PtdIns(4,5)P2] as well as phosphatidic acid (PtdA). Specifically, levels of [32P]PtdIns and [32P]PtdIns(4,5)P2 decreased rapidly (peak decrease at 10-15s), with a subsequent increase at 30 s and later. PtdIns4P and PtdA showed only an increase. In Me2SO-differentiated HL-60 cells prelabelled with [3H]inositol for 20 h, fMet-Leu-Phe caused a net increase in the cellular content of [3H]inositol phosphates, including a rapid increase in [3H]inositol 1,4,5-trisphosphate, suggesting that PtdIns(4,5)P2 breakdown occurs by a

phospholipase C mechanism. Both lysosomal enzyme secretion and changes in phospholipid metabolism occur over the same agonist concentration range with a similar time course. Binding of [3H]fMet-Leu-Phe, although occurring over the same concentration range, exhibited markedly slower kinetics. Although depletion of extracellular Ca2+ had no effect on **ligand**-induced polyphosphoinositide turnover, PtdIns turnover, PtdA labelling and lysosomal enzyme secretion were severely curtailed. These studies demonstrate a **receptor**-mediated enhancement of phospholipid turnover that correlates with a specific biological response to fMet-Leu-Phe. Further, the results are consistent with the idea that phospholipase C-mediated degradation of PtdIns(4,5)P2, which results in the formation of inositol trisphosphate, is an early step in the stimulus-secretion coupling pathway of the neutrophil. The lack of correlation between these two responses and the equilibrium-binding condition suggests that either these parameters are responsive to the rate of **ligand-receptor** interaction or only fractional occupation is required for a full biological response.

```
=> d his

     (FILE 'HOME' ENTERED AT 17:50:58 ON 18 MAY 2004)

     FILE 'MEDLINE, BIOSIS, EMBASE, SCISEARCH, CAPLUS, WPIDS' ENTERED AT
     17:51:26 ON 18 MAY 2004
L1       270426 S RECEPTOR AND LIGAND
L2           11 S L1 AND (FORMYLATED(A)PEPTIDE)
L3            6 DUP REM L2 (5 DUPLICATES REMOVED)

=> s l1 and multivalent
L4         1186 L1 AND MULTIVALENT

=> s l4 and G(a)protein
L5           42 L4 AND G(A) PROTEIN

=> dup rem
ENTER L# LIST OR (END):l5
PROCESSING COMPLETED FOR L5
L6           15 DUP REM L5 (27 DUPLICATES REMOVED)

=> d ibib abs l6 1-15

L6   ANSWER 1 OF 15  EMBASE  COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN                                                DUPLICATE 1
ACCESSION NUMBER:   2004105816  EMBASE
TITLE:              Extracellular Ca(2+) -sensing receptors - An overview.
AUTHOR:             Chang W.; Shoback D.
CORPORATE SOURCE:   W. Chang, Endocrine Research Unit, Department of Medicine,
                    University of California, San Francisco, CA, United States.
                    bambam@itsa.ucsf.edu
SOURCE:             Cell Calcium, (2004) 35/3 (183-196).
                    Refs: 138
                    ISSN: 0143-4160  CODEN: CECADV
COUNTRY:            United Kingdom
DOCUMENT TYPE:      Journal; General Review
FILE SEGMENT:       003     Endocrinology
                    005     General Pathology and Pathological Anatomy
                    022     Human Genetics
                    029     Clinical Biochemistry
LANGUAGE:           English
SUMMARY LANGUAGE:   English
AB   Extracellular Ca(2+)-sensing receptors (CaRs) are the molecular basis by
     which specialized cells detect and respond to changes in the extracellular
```

[Ca(2+)] ([Ca(2+)](o)). CaRs belong to the family C of **G-protein** coupled receptors (GPCRs). Activation of CaRs triggers signaling pathways that modify numerous cell functions. Multiple ligands regulate the activation of CaRs including **multivalent** cations, L-amino acids, and changes in ionic strength and pH. CaRs in parathyroid cells play a central role in systemic Ca(2+) homeostasis in terrestrial tetrapods. Mutations of the CaR gene in humans cause diseases in which serum and urine [Ca(2+)] and parathyroid hormone (PTH) levels are altered. CaR homologues are also expressed in organs critical to Ca(2+) transport in ancient and modern fish, suggesting that similar receptors may have long been involved in Ca(2+) homeostasis in lower vertebrates before parathyroid glands developed in terrestrial vertebrates. CaR mRNA and protein are also expressed in tissues not directly involved in Ca(2+) homeostasis. This implies that there may be other biological roles for CaRs. Studies of CaR-knockout mice confirm the importance of CaRs in the parathyroid gland and kidney. The functions of CaRs in tissues other than kidney and parathyroid gland, however, remain to be elucidated.

L6 ANSWER 2 OF 15 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-468779 [44] WPIDS
DOC. NO. NON-CPI: N2003-373023
DOC. NO. CPI: C2003-125210
TITLE: Quantifying analytes in solution using two or more **multivalent** proximity probes to respective binding site on analytes, with the proximity probes comprising 2-100 binding moieties and associated coupled nucleic acids.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): FREDRIKSSON, S
PATENT ASSIGNEE(S): (FRED-I) FREDRIKSSON S
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003044231	A1	20030530	(200344)*	EN	30
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
AU 2002353713	A1	20030610	(200419)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003044231	A1	WO 2002-SE2133	20021122
AU 2002353713	A1	AU 2002-353713	20021122

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002353713	A1 Based on	WO 2003044231

PRIORITY APPLN. INFO: SE 2002-1140 20020412; SE 2001-3905 20011123
AN 2003-468779 [44] WPIDS
AB WO2003044231 A UPAB: 20030710

NOVELTY - Detecting and/or quantifying analyte(s) (I) in solution, by binding two or more **multivalent** proximity probes (P) to respective binding site on (I), where (P) comprises 2-100 binding moieties (B) and associated coupled nucleic acid(s), allowing (B) to bind to (I) and allowing nucleic acids to interact with each other if they are in close proximity to each other, and detecting and/or quantifying degree of interaction between nucleic acids.

DETAILED DESCRIPTION - Detecting and/or quantifying one or more analyte(s) (I) in solution, involves binding two or more **multivalent** proximity probes (P) to a respective binding site on (I), where (P) comprise 2-100 binding moieties (B) and associated coupled nucleic acid(s), allowing (B) to bind to (I) and allowing the nucleic acids to interact with each other if they are in close proximity to each other, or detecting and/or quantifying degree of interaction between the nucleic acids, with the proviso that (B) and (I) do not all comprise nucleic acid.

An INDEPENDENT CLAIM is also included for a kit for detecting and quantifying one or more (I) in solution, comprising two or more **multivalent** proximity probes comprising 2-100 (B) with affinity for (I) and where each of the two **multivalent** proximity probes are associated with nucleic acid(s) capable of interacting.

USE - (M1) is useful for detecting and/or quantifying one or more analyte(s) e.**g. protein**(s), protein aggregate(s), prion(s) and/or nucleic acid(s). (M1) and the kit are useful for screening for **ligand-receptor** interaction antagonists in a high throughput screening procedure, for competitive detection and/or quantifying of a known or, an unknown analyte in solution, for screening **ligand** candidates in a large pool, for screening of drug candidates from large libraries, and for detection of infectious agents (claimed).

ADVANTAGE - The method increases the affinity of proximity probes through multivalency, and also provides an easier way to purify the proximity probes during manufacture. The method is rapid, sensitive and easy.

DESCRIPTION OF DRAWING(S) - The figure shows the example of **multivalent** proximity probe comprised of binding moieties backbone flexible polymer and reacting nucleic acid.

Dwg.3/8

L6 ANSWER 3 OF 15 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 2003-313086 [30] WPIDS

DOC. NO. CPI: C2003-082149

TITLE: Novel **multivalent** protein conjugate for treating a disease associated with abnormal angiogenesis, has multiple **ligand**-binding domains of different receptors.

DERWENT CLASS: B04 D16

INVENTOR(S): LIU, D; LIU, S; MARTINI, J

PATENT ASSIGNEE(S): (LIUD-I) LIU D; (LIUS-I) LIU S; (MART-I) MARTINI J; (ABMA-N) ABMAXIS INC

COUNTRY COUNT: 101

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003020906	A2	20030313	(200330)*	EN	115

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

US 2003064053 A1 20030403 (200330)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003020906	A2	WO 2002-US27888	20020830
US 2003064053	A1 Provisional	US 2001-316718P	20010831
		US 2002-232838	20020830

PRIORITY APPLN. INFO: US 2001-316718P 20010831; US 2002-232838 20020830

AN 2003-313086 [30] WPIDS

AB WO2003020906 A UPAB: 20030513

NOVELTY - A **multivalent** protein conjugate (I), comprising a number of multiple **ligand**-binding domains of different receptors, is new.

DETAILED DESCRIPTION - A **multivalent** protein conjugate (I) of formula (F1) to (F3).

BD1-L-(BD)n-2-L-BDn (F1)

BD = a **ligand**-binding domain of a **receptor**;

L = a covalent bond or a linker moiety; and

n = 2-50.

BD1-L-Tag-(BD)n-2-L-BDn (F2a)

BD1-L-(BD)n-2-Tag-L-BDn (F2b)

BD1-L-Tag-L-(BD)n-2-L-BDn (F2c)

Tag-BD1-L-Tag-L-(BD)n-2-L-BDn (F2d)

BD, L and n = as in (F1); and

Tag = a tag peptide sequence.

BD and n = as in (F1); and

L = a branched linker moiety.

ACTIVITY - Cytostatic; Vasotropic; Antiarteriosclerotic; Vulnerary; Cardiant; Antirheumatic; Antiarthritic; Gynecological; Antipsoriatic; Antidiabetic; Ophthalmological.

MECHANISM OF ACTION - Regulates angiogenesis; Inhibitor of endothelial cell growth.

Functional assessment for **multivalent** protein conjugate (2FT/A) was performed for its ability to inhibit endothelial cell proliferation stimulated by vasculoendothelial growth factor (VEGF). Briefly, from a subconfluent mono-layer of bovine brain capillary endothelial (BBE) cells, 12,500 cells were plated in 0.5 ml in a 24-well plate using a growth medium containing 10% calf serum (CS). After 24 hours, the growth medium was changed to 0.5% CS medium at 0.5 ml/well. After 18 hours of serum starvation, stimulating factors were added for 20 hours before pulsing cells with MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide). MTT was added at 1/10 final dilution (5 mg/ml stock solution) to each well and incubated for 3 hours in incubator. At the end of the incubation period, the medium was removed. The converted dye was solubilized with acidic isopropanol at 0.25 ml per well. Half of the solubilized precipitate was transferred into a 96-well plate and the absorbance measured at a wavelength of 570 nm with background subtraction at 660 nm. The results from the MTT assay showed that 2FT/A blocked the VEGF stimulated endothelial cell proliferation at 4 ng/ml and 8 ng/ml in vitro. The inhibitory effect was also dose-dependent. 2FT/A alone did not show any toxicity in the cell culture. The results demonstrated that the **ligand** binding domain of Flt1 (Flt1-D2) fused to that of Tie2 (Tie2-D1-3) can still exert its biological function by inhibiting VEGF-stimulated cell proliferation in vitro, which was comparable to the activity of an unfused Flt1-D2.

USE - (I) is useful for treating a disease associated with abnormal angiogenesis, including benign tumor (e.g. hemangioma, hepatocellular carcinoma and lipoma) or cancer (e.g. leukemia, breast cancer and prostate

cancer), restenosis, atherosclerosis, insults to body tissue due to surgery, abnormal wound healing, diseases that produce fibrosis or tissue, repetitive motion disorders, disorders of tissues that are not highly vascularized, and proliferative responses associated with organ transplants (claimed).

(I) is also useful for treating cardiovascular disorders, rheumatoid arthritis, ischemic-reperfusion related edema and injury, cortical ischemia, endometriosis, psoriasis, diabetic retinopathy, ocular angiogenic diseases, macular degeneration, neuroscular glaucoma, disorders associated with uncontrolled angiogenesis including retinal/choroidal neovascularization and corneal neovascularization.

DESCRIPTION OF DRAWING(S) - The figure shows a linear **multivalent** protein conjugate.

Dwg.1/5

L6 ANSWER 4 OF 15 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2004007595 EMBASE
TITLE: The CD81 Tetraspanin Facilitates Instantaneous Leukocyte VLA-4 Adhesion Strengthening to Vascular Cell Adhesion Molecule 1 (VCAM-1) under Shear Flow.
AUTHOR: Feigelson S.W.; Grabovsky V.; Shamri R.; Levy S.; Alon R.
CORPORATE SOURCE: R. Alon, Dept. of Immunology, Weizmann Institute of Science, Rehovot 76100, Israel. ronalon@wicc.weizmann.ac.il
SOURCE: Journal of Biological Chemistry, (19 Dec 2003) 278/51 (51203-51212).
Refs: 57
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Leukocyte integrins must rapidly strengthen their binding to target endothelial sites to arrest rolling adhesions under physiological shear flow. We demonstrate that the integrin-associated tetraspanin, CD81, regulates VLA-4 and VLA-5 adhesion strengthening in monocytes and primary murine B cells. CD81 strengthens **multivalent** VLA-4 contacts within subsecond integrin occupancy without altering intrinsic adhesive properties to low density **ligand**. CD81 facilitates both VLA-4-mediated leukocyte rolling and arrest on VCAM-1 under shear flow as well as VLA-5-dependent adhesion to fibronectin during short stationary contacts. CD81 also augments VLA-4 avidity enhancement induced by either chemokine-stimulated G(i) proteins or by protein kinase C activation, although it is not required for G(i) protein or protein kinase C signaling activities. In contrast to other proadhesive integrin-associated proteins, CD81-promoted integrin adhesiveness does not require its own **ligand** occupancy or ligation. These results provide the first demonstration of an integrin-associated transmembranal protein that facilitates instantaneous **multivalent** integrin occupancy events that promote leukocyte adhesion to an endothelial **ligand** under shear flow.

L6 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:819498 CAPLUS
DOCUMENT NUMBER: 139:322200
TITLE: The epidermal growth factor-like domains of the human EMR2 **receptor** mediate cell attachment through chondroitin sulfate glycosaminoglycans
AUTHOR(S): Stacey, Martin; Chang, Gin-Wen; Davies, John Q.; Kwakkenbos, Mark J.; Sanderson, Ralph D.; Hamann, Joerg; Gordon, Siamon; Lin, Hsi-Hsien
CORPORATE SOURCE: Sir William Dunn School of Pathology, University of

Oxford, UK
SOURCE: Blood (2003), 102(8), 2916-2924
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Using **multivalent** protein probes, an evolutionarily conserved endogenous **ligand** for EMR2, a human myeloid cell-restricted EGF-TM7 **receptor**, was identified on the surface of a number of adherent cell lines. In addition, in situ staining of the **ligand** has revealed specific in vivo patterns consistent with a connective tissue distribution. The interaction is conserved across species and mediated exclusively by the largest EMR2 isoform containing 5 epidermal growth factor (EGF)-like modules. Antibody-blocking studies subsequently revealed that the fourth EGF-like module constitutes the major **ligand**-binding site. The largest isoform of CD97, a related EGF-TM7 mol. containing an identical EGF-like module, also binds to the putative EMR2 **ligand** . Through the use of mutant Chinese hamster ovary (CHO) cell lines defective in glycosamino-glycans (GAGs) biosynthesis as well as the enzymic removal of specific cell surface GAGs, the mol. identity of the EMR2 **ligand** was identified as chondroitin sulfate (CS). Thus, exogenous CS GAGs blocked the EMR2-**ligand** interaction in a dose-dependent manner. EMR2-CS interaction is Ca2+- and sulphation-dependent and results in cell attachment. This is the first report of a GAG **ligand** for the TM7 receptors extending the already vast repertoire of stimuli of the GPCR superfamily.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 15 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2002406920 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12023293
TITLE: EMR4, a novel epidermal growth factor (EGF)-TM7 molecule up-regulated in activated mouse macrophages, binds to a putative cellular **ligand** on B lymphoma cell line A20.
AUTHOR: Stacey Martin; Chang Gin-Wen; Sanos Stephanie L; Chittenden Laura R; Stubbs Lisa; Gordon Siamon; Lin Hsi-Hsien
CORPORATE SOURCE: Sir William Dunn School of Pathology, University of Oxford, South Parks Road, Oxford, OX1 3RE, United Kingdom.
SOURCE: Journal of biological chemistry, (2002 Aug 9) 277 (32) 29283-93.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AY032690
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 20020806
Last Updated on STN: 20030105
Entered Medline: 20020909

AB A novel member of the EGF-TM7 family, mEMR4, was identified and characterized. The full-length mouse EMR4 cDNA encodes a predicted 689-amino acid protein containing two epidermal growth factor (EGF)-like modules, a mucin-like spacer domain, and a seven-transmembrane domain with a cytoplasmic tail. Genetic mapping established that mEMR4 is localized in the distal region of mouse chromosome 17 in close proximity to another EGF-TM7 gene, F4/80 (Emr1). Similar to F4/80, mEMR4 is predominantly expressed on resident macrophages. However, a much lower expression level was also detected in thioglycollate-elicited peritoneal neutrophils and bone marrow-derived dendritic cells. The expression of mEMR4 is up-regulated following macrophage activation in Biogel and

thioglycollate-elicited peritoneal macrophages. Similarly, mEMR4 is over-expressed in TNF-alpha-treated resident peritoneal macrophages, whereas interleukin-4 and -10 dramatically reduce the expression. mEMR4 was found to undergo proteolytic processing within the extracellular stalk region resulting in two protein subunits associated noncovalently as a heterodimer. The proteolytic cleavage site was identified by N-terminal amino acid sequencing and located at the conserved GPCR (**G protein**-coupled **receptor**) proteolytic site in the extracellular region. Using **multivalent** biotinylated mEMR4-mFc fusion proteins as a probe, a putative cell surface **ligand** was identified on a B lymphoma cell line, A20, in a cell-binding assay. The mEMR4-**ligand** interaction is Ca2+-independent and is mediated predominantly by the second EGF-like module. mEMR4 is the first EGF-TM7 **receptor** known to mediate the cellular interaction between myeloid cells and B cells.

L6 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2001:713652 CAPLUS
DOCUMENT NUMBER: 135:271869
TITLE: Methods and reagents for regulation of cellular responses in biological systems
INVENTOR(S): Kiessling, Laura L.; Strong, Laura E.; Gestwicki, Jason E.
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001071309	A2	20010927	WO 2001-US9174	20010321
WO 2001071309	A3	20030515		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001081499	A5	20011003	AU 2001-81499	20010321
US 2003125262	A1	20030703	US 2001-815296	20010321
EP 1334118	A2	20030813	EP 2001-959934	20010321
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004512258	T2	20040422	JP 2001-569247	20010321

PRIORITY APPLN. INFO.: US 2000-191014P P 20000321
WO 2001-US9174 W 20010321

AB This invention provides **multivalent** ligands which carry or display at least one recognition element (RE), and preferably a plurality of recognition elements, for binding directly or indirectly to cells or other biol. particles or more generally by binding to any biol. mol. The **multivalent** ligands provided can most generally function for binding or targeting to any biol. particle or mol. and particularly to targeting of cells or cell types or viruses, for cell aggregation and generally for macromol. assembly of biol. macromoleculares. The **multivalent** ligands of this invention are generally applicable for creating scaffolds (assemblies) of chemical or biol. species, including without limitation, antigens, epitopes, **ligand** binding groups,

ligands for cell receptors (cell surface receptors, transmembrane receptors and cytoplasmic receptors), various macromols. (nucleic acids, carbohydrates, saccharides, proteins, peptides, etc.). In these scaffolds, the number, spacing, relative positioning and relative orientation of recognition elements can be controlled. **Multivalent** ligands of this invention can carry or display at least one signal recognition element (SRE), and preferably a plurality of signal recognition elements, and modulate biol. responses in biol. systems. The invention also relates to methods for aggregating biol. particles and macromols. and for modulating biol. response employing the **multivalent** ligands provided.

L6 ANSWER 8 OF 15 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2001328384 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11279179
TITLE: Human epidermal growth factor (EGF) module-containing mucin-like hormone **receptor** 3 is a new member of the EGF-TM7 family that recognizes a **ligand** on human macrophages and activated neutrophils.
AUTHOR: Stacey M; Lin H H; Hilyard K L; Gordon S; McKnight A J
CORPORATE SOURCE: Sir William Dunn School of Pathology, University of Oxford, South Parks Road, Oxford OX1 3RE, United Kingdom.
SOURCE: Journal of biological chemistry, (2001 Jun 1) 276 (22) 18863-70.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF239764
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010730
Last Updated on STN: 20030105
Entered Medline: 20010726

AB The epidermal growth factor (EGF)-TM7 subgroup of **G-protein**-coupled receptors is composed predominantly of leukocyte-restricted glycoproteins defined by their unique hybrid structure, in which extracellular EGF-like domains are coupled to a seven-span transmembrane moiety via a mucin-like stalk. The EGF-TM7 group comprises mouse F4/80, human EGF module-containing mucin-like hormone **receptor** (EMR) 1, human EMR2, and human and mouse CD97, the genes for which map to human chromosome 19p13 and the syntenic regions of the mouse genome. In this study we describe the cloning and characterization of EMR3, a novel human EGF-TM7 molecule, and show the existence of its cellular **ligand**. The EMR3 gene maps closely to the existing members of the EGF-TM7 family on human chromosome 19p13.1 and, in common with other EGF-TM7 genes, is capable of generating different protein isoforms through alternative splicing. Two alternative splice forms have been isolated: one encoding a 652-amino acid cell surface protein consisting of two EGF-like domains, a mucin stalk, and a putative **G-protein**-coupled **receptor** domain and the other encoding a truncated soluble form containing only two EGF-like domains. As with other members of the EGF-TM7 family, EMR3 mRNA displays a predominantly leukocyte-restricted expression pattern, with highest levels in neutrophils, monocytes, and macrophages. Through the use of soluble EMR3 **multivalent** probes we have shown the presence of a **ligand** at the surface of monocyte-derived macrophages and activated human neutrophils. These interactions suggest a potential role for EMR3 in myeloid-myeloid interactions during immune and inflammatory responses.

L6 ANSWER 9 OF 15 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2001079317 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11114586
TITLE: Galactosyltransferase function during mammalian fertilization.
AUTHOR: Nixon B; Lu Q; Wassler M J; Foote C I; Ensslin M A; Shur B D
CORPORATE SOURCE: Department of Cell Biology, Emory University School of Medicine, Atlanta, GA 30322, USA.. barry@cellbio.emory.edu
SOURCE: Cells, tissues, organs, (2001) 168 (1-2) 46-57. Ref: 91
Journal code: 100883360. ISSN: 1422-6405.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010111

AB Gamete recognition has been studied extensively in the mouse. In this system, it is generally believed that sperm bind to a class of O-linked oligosaccharides on the zona pellucida glycoprotein, ZP3. The best characterized sperm **receptor** for ZP3 is beta1, 4-galactosyltransferase (GalT), which functions in a lectin-like capacity by binding to N-terminal N-acetylglucosamine residues on ZP3 oligosaccharides. **Multivalent** oligosaccharides on ZP3, as well as synthetic polymers terminating in N-acetylglucosamine aggregate GalT, leading to activation of a heterotrimeric **G protein** cascade and culminating in the acrosome reaction. Following fertilization, cortical granules release N-acetylglucosaminidase, which removes the binding site for sperm GalT and facilitates the zona block to polyspermic binding. Genetic manipulation of GalT expression has confirmed its function as a ZP3 **receptor**. Overexpressing GalT on sperm leads to increased binding of ZP3, increased **G protein** activation, and precocious acrosome reactions. In contrast, sperm from mice made null for GalT by homologous recombination are refractory to ZP3, in that they are unable to bind soluble ZP3 and fail to undergo the acrosome reaction in response to zona glycoproteins. Surprisingly, GalT null sperm still bind to the zona and achieve low rates of fertilization in vitro. This then suggests that sperm-egg binding involves **receptor-ligand** interactions independent of GalT and ZP3. The current model suggests that GalT functions as the ZP3 **receptor** that is responsible for inducing the acrosome reaction, whereas initial sperm-zona binding is dictated by other sperm surface receptors. Consistent with this, at least three other zona pellucida monosaccharides have been implicated in sperm binding, and novel sperm surface glycoproteins have been suggested to function in gamete binding. A large scaffolding protein has been identified that associates with the GalT cytoplasmic domain and may be responsible for orchestrating its signal transduction capacities that lead to the acrosome reaction.

L6 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:659896 CAPLUS
DOCUMENT NUMBER: 130:23092
TITLE: Is sperm galactosyltransferase a signaling subunit of a multimeric gamete **receptor**?
AUTHOR(S): Shur, Barry D.
CORPORATE SOURCE: Department of Cell Biology, Emory University School of Medicine, Atlanta, GA, 30322, USA
SOURCE: Biochemical and Biophysical Research Communications (1998), 250(3), 537-543
CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Academic Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB This is a review with 79 refs. on mol. aspect of gamete recognition in mammalian fertilization. One of the **receptor-ligand** interactions that facilitates gamete recognition is the binding of an N-acetylglucosamine (GlcNAc) residue on ZP3 to a sperm surface galactosyltransferase (GalT). The binding of multiple GlcNAc residues, presented by **multivalent** oligosaccharide chains, leads to an aggregation of GalT, activating a heterotrimeric **G-protein** cascade that is associated with the GalT cytoplasmic domain. Since sperm from GalT-null mice still bind to the zona pellucida (although without undergoing an acrosome reaction), other zona ligands, either on ZP3 or other zona glycoproteins, likely bind to sperm receptors adjacent to GalT, which together form a multimeric **receptor** complex. (c) 1998 Academic Press.
REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 15 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 1998328569 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9665632
TITLE: Modelling human sperm-egg interactions in vitro: signal transduction pathways regulating the acrosome reaction.
AUTHOR: Benoff S
CORPORATE SOURCE: Department of Obstetrics and Gynecology, North Shore University Hospital-New York University Medical College, Manhasset 11030, USA.
CONTRACT NUMBER: ES 06100 (NIEHS)
SOURCE: Molecular human reproduction, (1998 May) 4 (5) 453-71.
Ref: 239
Journal code: 9513710. ISSN: 1360-9947.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19981029
Last Updated on STN: 20000303
Entered Medline: 19981022
AB Recent advances in characterizing sperm surface receptors and ion channels, when combined with the rapidly expanding knowledge of interactions among second messenger systems in somatic cells, permit formulation of a tentative molecular mechanism for the regulation of the human sperm acrosome reaction. As spermatozoa pass through the cumulus mass, progesterone binds to its sperm surface **receptor,** alkalinizes the sperm head cytosol and potentiates changes in intracellular ionized calcium. Primary binding of spermatozoa to egg involves receptors for mannosyl, N-acetylglucosaminyl and, possibly, fucosyl residues of the glycosylated zona protein, ZP3. These receptors aggregate on **multivalent ligand** binding, migrate to the equatorial region along an actin filament network formed between the plasma and acrosomal membranes during capacitation, and activate a **G protein**/protein kinase A/protein kinase C second messenger system and a secondary proteolysis signal. Binding of a **receptor** tyrosine kinase to ZP3 amino acid residues simultaneous with the sugar recognition event triggers tyrosine phosphorylation signalling. All signals combine to open a voltage-dependent calcium channel. The resulting elevated calcium signal depolymerizes the inter-membrane actin network and activates phospholipases, leading to an acrosome reaction.

L6 ANSWER 12 OF 15 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 1998075020 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9414209
TITLE: Calculation of diffusion-limited kinetics for the reactions in collision coupling and **receptor** cross-linking.
AUTHOR: Shea L D; Omann G M; Linderman J J
CORPORATE SOURCE: Department of Chemical Engineering, University of Michigan, Ann Arbor 48109, USA.
SOURCE: Biophysical journal, (1997 Dec) 73 (6) 2949-59.
Journal code: 0370626. ISSN: 0006-3495.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980217
Last Updated on STN: 20000303
Entered Medline: 19980205

AB Both enzyme (e.g., **G-protein**) activation via a collision coupling model and the formation of cross-linked receptors by a **multivalent ligand** involve reactions between two molecules diffusing in the plasma membrane. The diffusion of these molecules is thought to play a critical role in these two early signal transduction events. In reduced dimensions, however, diffusion is not an effective mixing mechanism; consequently, zones in which the concentration of particular molecules (e.g., enzymes, receptors) becomes depleted or enriched may form. To examine the formation of these depletion/accumulation zones and their effect on reaction rates and ultimately the cellular response, Monte Carlo techniques are used to simulate the reaction and diffusion of molecules in the plasma membrane. The effective reaction rate at steady state is determined in terms of the physical properties of the tissue and **ligand** for both enzyme activation via collision coupling and the generation of cross-linked receptors. The diffusion-limited reaction rate constant is shown to scale with the mean square displacement of a **receptor-ligand** complex. The rate constants determined in the simulation are compared with other theoretical predictions as well as experimental data.

L6 ANSWER 13 OF 15 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 97113278 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8807885
TITLE: Synthesis and characterization of bivalent peptide ligands targeted to **G-protein**-coupled receptors.
AUTHOR: Carrithers M D; Lerner M R
CORPORATE SOURCE: Department of Neurology, Yale University School of Medicine, New Haven, CT 06520-8024, USA. MRLERNER@aol.com
SOURCE: Chemistry & biology, (1996 Jul) 3 (7) 537-42.
Journal code: 9500160. ISSN: 1074-5521.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970305
Last Updated on STN: 20000303
Entered Medline: 19970219

AB BACKGROUND: Through the effects of avidity, multivalency can increase the apparent affinity of a **ligand** for its binding site. Low molecular weight, high affinity, **multivalent** ligands theoretically could be used to deliver a variety of agents to specific cell subtypes. In order to target specific **G-protein**

-coupled receptors, a series of monospecific peptide dimers were synthesized that are designed to bind to two adjacent **receptor** sites. RESULTS: Three dimers, consisting of a **ligand** region, a short, flexible, uncharged spacer, a longer, polylysine spacer and a single cysteine residue to permit dimerization, and the corresponding monomers were synthesized by solid-phase peptide synthesis. The **ligand** domain was either alpha-melanocyte stimulating hormone (alpha-MSH), an alpha-MSH **receptor** antagonist (alpha-MSH-ANT), or bombesin. These ligands were characterized in a functional melanocyte dispersion assay. In wild-type melanophores, the alpha-MSH dimer stimulated dispersion with an EC50 approximately seven-fold lower than that of the corresponding monomer. Similarly, in cells transfected with bombesin **receptor** cDNA, the bombesin dimer was approximately five-fold more potent than the monomer. The alpha-MSH-ANT monomer specifically inhibited alpha-MSH-mediated dispersion with no significant agonist activity, but the dimer acted predominantly as an agonist. CONCLUSIONS: Peptide dimers can be synthesized easily and have enhanced functional activity; monospecific dimers have greater avidity and bispecific dimers are likely to have greater selectivity. They may therefore have practical potential as specific cell-targeting agents.

L6 ANSWER 14 OF 15 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 96010001 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7569899
TITLE: Activation of a **G protein** complex by aggregation of beta-1,4-galactosyltransferase on the surface of sperm.
AUTHOR: Gong X; Dubois D H; Miller D J; Shur B D
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, University of Texas M.D. Anderson Cancer Center, Houston 77030, USA.
CONTRACT NUMBER: RO1 HD22590 (NICHD)
RO1 HD23479 (NICHD)
T32 HD07324 (NICHD)
+
SOURCE: Science, (1995 Sep 22) 269 (5231) 1718-21.
Journal code: 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199510
ENTRY DATE: Entered STN: 19951227
Last Updated on STN: 20021218
Entered Medline: 19951025

AB Fertilization is initiated by the species-specific binding of sperm to the extracellular coat of the egg. One sperm **receptor** for the mouse egg is beta-1,4-galactosyltransferase (GalTase), which binds O-linked oligosaccharides on the egg coat glycoprotein ZP3. ZP3 binding induces acrosomal exocytosis through the activation of a pertussis toxin-sensitive heterotrimeric guanine nucleotide-binding **protein** (**G protein**). The cytoplasmic domain of sperm surface GalTase bound to and activated a heterotrimeric **G protein** complex that contained the Gi alpha subunit. Aggregation of GalTase by **multivalent** ligands elicited **G protein** activation. Sperm from transgenic mice that overexpressed GalTase had higher rates of **G protein** activation than did wild-type sperm, which rendered transgenic sperm hypersensitive to their ZP3 **ligand**. Thus, the cytoplasmic domain of cell surface GalTase appears to enable it to function as a signal-transducing **receptor** for extracellular oligosaccharide ligands.

L6 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1994:296470 CAPLUS
DOCUMENT NUMBER: 120:296470
TITLE: Dual pertussis toxin-sensitive pathway of zymosan-induced activation in guinea pig macrophages. An anti-CR3 antibody-inhibitable stimulation of phagocytosis and -resistant stimulation of O2- production and arachidonate release
AUTHOR(S): Hazeki, Kaoru; Tamoto, Koichi; Ui, Michio; Mori, Yoki
CORPORATE SOURCE: Department of Microbiology, Faculty of Pharmaceutical Sciences, Higashi-Nippon-Gakuen University, Ishikari-Tobetsu, 061-02, Japan
SOURCE: FEBS Letters (1994), 342(1), 29-32
CODEN: FEBLAL; ISSN: 0014-5793
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Complement **receptor** type 3 (CR3)-mediated cellular responses in guinea pig macrophages were investigated by using zymosan and serum-opsonized zymosan (SOZ) as the **multivalent ligand** for CR3. The ingestion of zymosan and SOZ was accompanied by O2- generation and arachidonate release. These responses were suppressed by prior exposure of macrophages to pertussis toxin (PT). Opsonization of zymosan gave rise to more than 6-fold activation of the ingestion, whereas the magnitude of either arachidonate release or O-2 generation was unchanged. The Fab' fragment of anti-Z-1, a monoclonal antibody specific for the α chain of guinea pig CR3, inhibited the ingestion of zymosan by 60% without affecting zymosan-induced arachidonate release and O2- generation. These data suggested that there might be at least two functionally distinct binding sites for zymosan. O2- generation and arachidonate release might be regulated through one site and phagocytosis another. Both sites should be coupled to PT-sensitive GTP binding protein.

=> d his

(FILE 'HOME' ENTERED AT 17:50:58 ON 18 MAY 2004)

FILE 'MEDLINE, BIOSIS, EMBASE, SCISEARCH, CAPLUS, WPIDS' ENTERED AT 17:51:26 ON 18 MAY 2004
L1 270426 S RECEPTOR AND LIGAND
L2 11 S L1 AND (FORMYLATED(A)PEPTIDE)
L3 6 DUP REM L2 (5 DUPLICATES REMOVED)
L4 1186 S L1 AND MULTIVALENT
L5 42 S L4 AND G(A)PROTEIN
L6 15 DUP REM L5 (27 DUPLICATES REMOVED)

=> s l1 and G(a)protein
L7 16240 L1 AND G(A) PROTEIN

=> s l4 and ((T(a)cell) or (B(a)cell) or neutrophil or lymphocyte or leukocyte or epithelial or endothelial)
L8 312 L4 AND ((T(A) CELL) OR (B(A) CELL) OR NEUTROPHIL OR LYMPHOCYTE OR LEUKOCYTE OR EPITHELIAL OR ENDOTHELIAL)

=> s l8 and (scaffold or scaffolding or array or arrays)
L9 20 L8 AND (SCAFFOLD OR SCAFFOLDING OR ARRAY OR ARRAYS)

=> dup rem l9
PROCESSING COMPLETED FOR L9
L10 9 DUP REM L9 (11 DUPLICATES REMOVED)

=> d ibib abs l10 1-9

L10 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:539861 CAPLUS
DOCUMENT NUMBER: 137:90571
TITLE: Compositions and methods for regulating **receptor** clustering
INVENTOR(S): Dennis, Jim; Demetriou, Michael
PATENT ASSIGNEE(S): Mount Sinai Hospital, Can.
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002055728	A2	20020718	WO 2002-CA2	20020111
WO 2002055728	A3	20030515		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004082009	A1	20040429	US 2003-250935	20031215

PRIORITY APPLN. INFO.: US 2001-261516P P 20010112
WO 2002-CA2 W 20020111

AB The invention relates to isolated complexes comprising one or more galectin associated with a Mgat5 modified glycan or polylactosamine modified glycan, and isolated lectin-Mgt5 modified glycan lattice comprising an **array** of **multivalent** interactions among lectins, Mgat5 modified glycans, polylactosamine modified glycans, and/or glycoproteins. Methods for evaluating a test compound for its ability to regulate **receptor** clustering through glycans on cell surfaces; and methods for regulating **receptor** clustering on cell surfaces comprising altering glycans on the cell surface associated with **receptor** clustering are also disclosed. Mgat5-deficient mice displayed kidney autoimmune disease, enhanced delayed type hypersensitivity, and increased susceptibility to exptl. autoimmune encephalomyelitis. Mgat5 deficiency lowered **T cell** activation thresholds by directly enhancing TCR clustering.

L10 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:168664 CAPLUS
DOCUMENT NUMBER: 137:291067
TITLE: Cell Aggregation by Scaffolded **Receptor** Clusters
AUTHOR(S): Gestwicki, Jason E.; Strong, Laura E.; Cairo, Christopher W.; Boehm, Frederick J.; Kiessling, Laura L.
CORPORATE SOURCE: Department of Biochemistry, University of Wisconsin-Madison, Madison, WI, 53706, USA
SOURCE: Chemistry & Biology (2002), 9(2), 163-169
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aggregation of cells by lectins or antibodies is important for biotechnol. and therapeutic applications. One strategy to augment the

avidity and aggregating properties of these mediators is to maximize the number of their **ligand** binding sites. The valency of lectins and antibodies, however, is limited by their quaternary structures. To overcome this limitation, we explored the use of polymers generated by ring-opening metathesis polymerization (ROMP) as scaffolds to noncovalently assemble multiple copies of a lectin, the tetravalent protein Con A (Con A). We demonstrate that complexes between Con A and **multivalent** scaffolds aggregate cells of a **T cell** leukemia line (Jurkat) more effectively than Con A alone. We anticipate that synthetic scaffolds will offer a new means of facilitating processes that rely on cell aggregation, such as pathogen clearance and immune recognition.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2001:713652 CAPLUS
DOCUMENT NUMBER: 135:271869
TITLE: Methods and reagents for regulation of cellular responses in biological systems
INVENTOR(S): Kiessling, Laura L.; Strong, Laura E.; Gestwicki, Jason E.
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001071309	A2	20010927	WO 2001-US9174	20010321
WO 2001071309	A3	20030515		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001081499	A5	20011003	AU 2001-81499	20010321
US 2003125262	A1	20030703	US 2001-815296	20010321
EP 1334118	A2	20030813	EP 2001-959934	20010321
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004512258	T2	20040422	JP 2001-569247	20010321

PRIORITY APPLN. INFO.: US 2000-191014P P 20000321
WO 2001-US9174 W 20010321

AB This invention provides **multivalent** ligands which carry or display at least one recognition element (RE), and preferably a plurality of recognition elements, for binding directly or indirectly to cells or other biol. particles or more generally by binding to any biol. mol. The **multivalent** ligands provided can most generally function for binding or targeting to any biol. particle or mol. and particularly to targeting of cells or cell types or viruses, for cell aggregation and generally for macromol. assembly of biol. macromoleculares. The **multivalent** ligands of this invention are generally applicable for creating scaffolds (assemblies) of chemical or biol. species, including without limitation, antigens, epitopes, **ligand** binding groups, ligands for cell receptors (cell surface receptors, transmembrane receptors and cytoplasmic receptors), various macromols. (nucleic acids,

carbohydrates, saccharides, proteins, peptides, etc.). In these scaffolds, the number, spacing, relative positioning and relative orientation of recognition elements can be controlled. **Multivalent** ligands of this invention can carry or display at least one signal recognition element (SRE), and preferably a plurality of signal recognition elements, and modulate biol. responses in biol. systems. The invention also relates to methods for aggregating biol. particles and macromols. and for modulating biol. response employing the **multivalent** ligands provided.

L10 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:382922 CAPLUS
DOCUMENT NUMBER: 134:55245
TITLE: Monitoring antigen-specific T cells using MHC-Ig dimers
AUTHOR(S): Schneck, Jonathan P.
CORPORATE SOURCE: School of Medicine, Departments of Oncology and Pathology, Johns Hopkins University, Baltimore, MD, USA
SOURCE: Immunological Investigations (2000), 29(2), 163-169
CODEN: IMINEJ; ISSN: 0882-0139
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two novel approaches are currently being examined that allow for the identification of antigen-specific T cells. A biochem. approach to generating soluble **multivalent** MHC complexes has been to generate tetrameric MHC complexes linked to avidin. A general approach for producing soluble divalent versions of class I and class II MHC mols., using Ig as a mol. **scaffold**, has also been developed. An exptl. system is presented which outlines a general approach of using **multivalent** high affinity ligands to study cell-cell interactions, driven by **multivalent ligand-receptor** interactions. Divalent chimeric mols. were found to be high-avidity analogs of proteins useful in probing and selectively regulating cellular responses.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 9 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1999235242 EMBASE
TITLE: In vivo **ligand** specificity of E-selectin binding to **multivalent** sialyl lewis N-linked oligosaccharides.
AUTHOR: Thomas V.H.; Yang Y.; Rice K.G.
CORPORATE SOURCE: K.G. Rice, College of Pharmacy, University of Michigan, 428 Church St., Ann Arbor, MI 48109-1065, United States. krice@mich.edu
SOURCE: Journal of Biological Chemistry, (2 Jul 1999) 274/27 (19035-19040).
Refs: 40
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The in vivo specificity for E-selectin binding to a panel of N-linked oligosaccharides containing a clustered **array** of one to four sialyl Lewis(x) (SLe(x); NeuAcα2-3Gal[Fucα1-3]β1-4GlcNAc) determinants was studied in mice. Following intraperitoneal dosing with lipopolysaccharide, radioiodinated tyrosinamide N-linked oligosaccharides

were dosed i.v. and analyzed for their pharmacokinetics and biodistribution. Specific targeting was determined from the degree of SLe(x) oligosaccharide targeting relative to a sialyl oligosaccharide control. Oligosaccharides targeted the kidney with the greatest selectivity after a 4-h induction period following lipopolysaccharide dosing. Unique pharmacokinetic profiles were identified for SLe(x) biantennary and triantennary oligosaccharides but not for monovalent and tetraantennary SLe(x) oligosaccharides or sialyl oligosaccharide controls. Biodistribution studies established that both SLe(x) biantennary and triantennary oligosaccharides distributed to the kidney with 2-3-fold selectivity over sialyl oligosaccharide controls, whereas monovalent and tetraantennary SLe(x) oligosaccharides failed to mediate specific kidney targeting. Simultaneous dosing of SLe(x) biantennary or triantennary oligosaccharide with a mouse anti-E-selectin monoclonal antibody blocked kidney targeting, whereas co-administration with anti-P- selectin monoclonal antibody did not significantly block kidney targeting. The results suggest that SLe(x) biantennary and triantennary are N-linked oligosaccharide ligands for E-selectin and implicate E-selectin as a bivalent **receptor** in the murine kidney endothelium.

L10 ANSWER 6 OF 9 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1997-012213 [01] WPIDS
DOC. NO. NON-CPI: N1997-010560
DOC. NO. CPI: C1997-003453
TITLE: Specific inhibitors of interaction between **T cell receptor** and MHC peptide **ligand** - identified by incubating **receptor** expressing cells with **ligand** and test cpd., and measuring change in interaction to detect cpds. potentially useful for blocking disease related T cells.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): BAROUCH, D H; JAKOBSEN, B K; VESSEY, S J R
PATENT ASSIGNEE(S): (CANC-N) CANCER RES CAMPAIGN TECHNOLOGY
COUNTRY COUNT: 70
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9636881	A2	19961121	(199701)*	EN	21
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG					
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN					
AU 9657690	A	19961129	(199712)		
WO 9636881	A3	19970109	(199713)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9636881	A2	WO 1996-GB1165	19960516
AU 9657690	A	AU 1996-57690	19960516
WO 9636881	A3	WO 1996-GB1165	19960516

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9657690	A	Based on	WO 9636881

PRIORITY APPLN. INFO: GB 1995-9844 19950516

AN 1997-012213 [01] WPIDS
AB WO 9636881 A UPAB: 19970102
Novel specific inhibitors of the interaction between a **T-cell receptor** (TCR) and a MHC peptide **ligand** (L), are identified by: (a) incubating responder cells that express TCR with a L which stimulates the cells, and a test cpd.; (b) monitoring a signal produced by the cell when TCR and L interact; and (c) comparing this signal with a control signal from a similar system lacking the test cpd.. Also new is a multimerised **multivalent array** of MHC mols. for use in the method.

USE - The specific inhibitors are potentially useful for blocking T-cells that cause autoimmune diseases (e.g. diabetes, rheumatoid arthritis, Grave's disease etc.), organ transplant rejection or other **T cell** mediated conditions.

Dwg.2/4

L10 ANSWER 7 OF 9 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 95123068 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7529792
TITLE: **Multivalent**, but not divalent, antigen **receptor** cross-linkers synergize with CD40 **ligand** for induction of Ig synthesis and class switching in normal murine B cells. A redefinition of the TI-2 vs **T cell**-dependent antigen dichotomy.
AUTHOR: Snapper C M; Kehry M R; Castle B E; Mond J J
CORPORATE SOURCE: Department of Pathology, Uniformed Services University of the Health Sciences, Bethesda, MD 20814.
CONTRACT NUMBER: AI32560 (NIAID)
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (1995 Feb 1) 154 (3) 1177-87.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199502
ENTRY DATE: Entered STN: 19950223
Last Updated on STN: 19960129
Entered Medline: 19950216

AB A number of previous studies have suggested that cross-linkage of the **B cell** Ag **receptor** may be critical for induction of humoral immune responses to **T cell**-dependent (TD) Ags in vivo. Previous work also indicated a critical role, in these responses, for CD40-mediated signaling mediated by binding of the inducible **T cell** membrane protein, CD40 **ligand** (CD40L). Data in this manuscript demonstrate that concentrations of bivalent anti-IgD or anti-IgM Ab as high as 30 micrograms/ml induced little if any enhancement of CD40-dependent Ig secretion by resting murine B cells. In contrast, concentrations as low as 3 pg/ml of **multivalent**, dextran-conjugated, anti-IgD (alpha delta-dex) or anti-IgM (alpha mu-dex) were strongly synergistic with CD40L for induction of **B cell** proliferation, viable cell outgrowth, Ig isotype switching, and maturation to Ig secretion. As many as 30% of the B cells became membrane IgG1+ after stimulation with CD40L, anti-Ig-dextran, and IL-4 + IL-5, with a concomitant three- to fivefold increase in numbers of viable cells as compared with control cultures. High Ig secretory responses were obtained in response to the combined actions of CD40L and alpha delta-dex or alpha mu-dex, utilizing concentrations of **B cell** activator that when acting alone induced only modest Ig secretion. Surprisingly, although we previously demonstrated that alpha delta-dex selectively and strongly suppressed IgE production by **T cell**-activated B cells,

it strikingly augmented IgE expression by CD40L-activated B cells. These data suggest 1) a key role for Ag **receptor** cross-linkage in CD40-dependent induction of humoral immune responses, 2) that to achieve a membrane Ig-dependent enhancing effect in the presence of activated T cells, TD Ags must be displayed to the **B cell** as a **multivalent array** of epitopes, 3) that picomolar concentrations of Ag can mediate this effect, and 4) that at least for induction of IgE responses, **B cell** stimulation via CD40L or via activated T cells may lead to a qualitatively different pathway of activation.

L10 ANSWER 8 OF 9 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 93018871 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1402685
TITLE: Inhibition or activation of human **T cell receptor** transfectants is controlled by defined, soluble antigen **arrays**.
AUTHOR: Symer D E; Dintzis R Z; Diamond D J; Dintzis H M
CORPORATE SOURCE: Department of Biophysics and Biophysical Chemistry, Johns Hopkins University School of Medicine, Baltimore, Maryland 21205.
CONTRACT NUMBER: GM-07309 (NIGMS)
SOURCE: Journal of experimental medicine, (1992 Nov 1) 176 (5) 1421-30.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199211
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19930122
Entered Medline: 19921125

AB We present evidence that direct **T cell receptor** (TCR) occupancy by antigen can either activate or inhibit T cells, depending upon whether or not a threshold number of local TCRs are crosslinked by **multivalent arrays** of the antigen. Variants of Jurkat cells were previously transfected with TCR alpha and beta chains that bind fluorescein, yielding FL-TCR+ human T cells. The transfectants are activated upon binding soluble **multivalent** antigen **arrays** at concentrations well below those required for monovalent interactions. This activation, measured by calcium fluxes and interleukin 2 (IL-2) production, indicates the superior binding avidity of **multivalent** ligands. Smaller, less **multivalent** **arrays** do not activate the cells, but antagonize larger **arrays**, demonstrating that antigen can bind TCR as either agonist or antagonist. The balance between activation and inhibition depends upon antigen **array** size, **ligand** valence, and concentration, indicating that a threshold extent of **receptor** crosslinking, and not individual perturbations of single TCR, is required for activation by antigen. Approximately 100 stimulatory **arrays** specifically bind per FL-TCR+ cell at concentrations where IL-2 production is half-maximal.

L10 ANSWER 9 OF 9 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 86197760 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2422265
TITLE: Role of L3T4 and Ia in the heteroclitic response of T cells to cytochrome c.
AUTHOR: Lakey E K; Margoliash E; Fitch F W; Pierce S K
CONTRACT NUMBER: AI 12001 (NIAID)
AI 18939 (NIAID)
GM 19121 (NIGMS)
+

SOURCE: Journal of immunology (Baltimore, Md. : 1950), (1986 Jun 1) 136 (11) 3933-8.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198606
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19970203
Entered Medline: 19860613

AB The activation of helper T lymphocytes has been proposed to result from the sum of low-affinity interactions between the specific immune **receptor**, as well as nonpolymorphic receptors such as L3T4 on the **T cell** surface, and nominal antigen and Ia displayed in a **multivalent array** on the antigen-presenting cell surface. The present work takes advantage of a **T cell** hybridoma specific for pigeon cytochrome c in the context of I-Ek, which responds to tobacco hornworm moth cytochrome c at one hundredth the concentration of the homologous antigen, to determine if the **T cell**'s requirement for L3T4 and Ia is directly related to its functional affinity for antigen. The results demonstrate that the **T cell**'s activation by pigeon cytochrome c was blocked by antibodies directed to L3T4 and to I-Ek, even at antigen concentrations twofold to fourfold above those required for maximal responses. In contrast, the response to tobacco hornworm moth cytochrome c was not as affected by these antibodies under equivalent superoptimal conditions. The same phenomenon was observed for the **T cell**'s activation by the carboxyl-terminal peptide fragments of the two cytochromes c, which do not require processing, indicating that the differences were not due to the relative efficiency of processing and/or presentation of the antigens. Although both I-Ek- and L3T4-specific antibodies blocked the **T cell** response to pigeon cytochrome, antibodies to I-Ak had no effect, even though I-Ak had been considered to be a **ligand** for L3T4. Thus, either Ia does not bind L3T4 or, if it does, I-Ek must be a sufficient **ligand** for L3T4 for T cells that recognize their antigen in the context of I-Ek. These studies provide more definitive evidence that the **T cell**'s requirement for the functions of Ia and of L3T4 is dependent on the **T cell**'s functional affinity for its antigenic determinant. This data is consistent with a model of **T cell** activation in which, given a high enough affinity of the **T cell receptor** for the processed antigen, the requirement for other components of a stimulatory complex, such as Ia and L3T4, may diminish to undetectable levels.

=> d his

(FILE 'HOME' ENTERED AT 17:50:58 ON 18 MAY 2004)

FILE 'MEDLINE, BIOSIS, EMBASE, SCISEARCH, CAPLUS, WPIDS' ENTERED AT 17:51:26 ON 18 MAY 2004

L1 270426 S RECEPTOR AND LIGAND
L2 11 S L1 AND (FORMYLATED(A)PEPTIDE)
L3 6 DUP REM L2 (5 DUPLICATES REMOVED)
L4 1186 S L1 AND MULTIVALENT
L5 42 S L4 AND G(A)PROTEIN
L6 15 DUP REM L5 (27 DUPLICATES REMOVED)
L7 16240 S L1 AND G(A)PROTEIN
L8 312 S L4 AND ((T(A)CELL) OR (B(A)CELL) OR NEUTROPHIL OR LYMPHOCYTE
L9 20 S L8 AND (SCAFFOLD OR SCAFFOLDING OR ARRAY OR ARRAYS)
L10 9 DUP REM L9 (11 DUPLICATES REMOVED)

```
=> s l1 and (derivatized(a)peptide)
L11          9 L1 AND (DERIVATIZED(A) PEPTIDE)

=> dup rem l11
PROCESSING COMPLETED FOR L11
L12          4 DUP REM L11 (5 DUPLICATES REMOVED)

=> d ibib abs l12 1-4

L12  ANSWER 1 OF 4  WPIDS  COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER:     2003-177680 [18]   WPIDS
DOC. NO. NON-CPI:     N2003-139756
DOC. NO. CPI:         C2003-046935
TITLE:                Device for presenting polypeptides, useful as protein
                      chip e.g. for immunoassays, comprises polypeptide linked
                      to carrier through semicarbazone bond.
DERWENT CLASS:        B04 D16 S03
INVENTOR(S):          AURIAULT, C; BOUZIDI, A; DUBURCQ, X; DURAND, J O; GRAS, M
                      H; MELNYK, O; OLIVIER, C; DURAND, J; EL-MAHDI, O; GARCIA,
                      J; GRAS-MASSE, H
PATENT ASSIGNEE(S):   (CNRS) CNRS CENT NAT RECH SCI; (INSP) INST PASTEUR LILLE;
                      (SEDA-N) SEDAC THERAPEUTICS SOC ETUD DEV ANTIGENE;
                      (UYLI-N) UNIV LILLE II; (SEDA-N) SEDAC SOC ETUD & DEV
                      ANTIGENES COMBINATO; (UYLI-N) UNIV LILLE 2 DROIT & SANTE
COUNTRY COUNT:        101
PATENT INFORMATION:

     PATENT NO        KIND DATE     WEEK      LA   PG
     ---------------------------------------------
     FR 2825095       A1 20021129 (200318)*      44
     WO 2002097442    A2 20021205 (200318)  FR
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
            NL OA PT SD SE SL SZ TR TZ UG ZM ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
            KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
            RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM
            ZW
     EP 1390751       A2 20040225 (200415)  FR
         R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
            RO SE SI TR

APPLICATION DETAILS:

     PATENT NO      KIND                  APPLICATION          DATE
     ---------------------------------------------------------------
     FR 2825095     A1                    FR 2001-6931         20010528
     WO 2002097442  A2                    WO 2002-FR1771       20020527
     EP 1390751     A2                    EP 2002-740818       20020527
                                          WO 2002-FR1771       20020527

FILING DETAILS:

     PATENT NO       KIND                  PATENT NO
     ---------------------------------------------
     EP 1390751      A2 Based on           WO 2002097442

PRIORITY APPLN. INFO: FR 2001-6931          20010528
AN   2003-177680 [18]   WPIDS
AB   FR   2825095 A UPAB: 20030317
     NOVELTY - Device (A) for presentation of polypeptides (I), useful as a
     chip for miniaturized detection of structurally or functionally
```

complementary molecules. It comprises a flat support on which (I) are covalently fixed by formation of a semicarbazone bond.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method of preparing (A).

USE - (A) are useful as polypeptide chips for diagnosis (particularly based on antigen-antibody reactions), for screening compounds, and for analysis of reactions of the **receptor-ligand** type.

ADVANTAGE - Semicarbazide groups can be attached at high (and variable) density, homogeneously and reproducibly, ensuring better sensitivity and very low background (excellent signal-to-noise ratio), particularly when used with samples that contain other proteins.

Dwg.0/4

L12 ANSWER 2 OF 4 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2002399749 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12148786
TITLE: CCK8 **peptide derivatized** with diphenylphosphine for rhenium labelling: synthesis and molecular mechanics calculations.
AUTHOR: Morelli Giancarlo; De Luca Stefania; Tesauro Diego; Saviano Michele; Pedone Carlo; Dolmella Alessandro; Visentin Roberta; Mazzi Ulderico
CORPORATE SOURCE: Centro Interuniversitario per la Ricerca sui Peptidi Bioattivi e Istituto du Biostrutture e Bioimmagini, CNR, Napoli, Italy.. morelli@chemistry.unina.it
SOURCE: Journal of peptide science : an official publication of the European Peptide Society, (2002 Jul) 8 (7) 373-81.
Journal code: 9506309. ISSN: 1075-2617.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20020801
Last Updated on STN: 20030131
Entered Medline: 20030130

AB A novel CCK8 derivative bearing a chelating agent at its N- end and its oxo-rhenium(V) complex have been synthesized and characterized. The chelating agent N-[N-13-(diphenylphosphino)propionyl]glycyl]cysteine (PN2S) **ligand**, the coordination set of which is made by the phosphorus atom of phosphine, the nitrogen atoms of the two amido groups and the sulphur atom of cysteine, has been used due to its high affinity towards the oxo-rhenium(V) moiety. Molecular modelling studies indicate that the CCK8 peptide adopts the right conformation for cholecystokinin **receptor** binding, and that modifications on the N-terminal side of CCK8 obtained by introducing chelating agents and its metal complexes should not affect the interaction with CCK(A) **receptor**.

L12 ANSWER 3 OF 4 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 97:389850 SCISEARCH
THE GENUINE ARTICLE: WZ027
TITLE: Protein a mimetic peptide **ligand** for affinity purification of antibodies
AUTHOR: Fassina G (Reprint); Verdoliva A; Odierna M R; Ruvo M; Cassini G
CORPORATE SOURCE: TECNOGEN SCPA, I-81015 PIANA MONTE VERNA, CE, ITALY
COUNTRY OF AUTHOR: ITALY
SOURCE: JOURNAL OF MOLECULAR RECOGNITION, (SEP-DEC 1996) Vol. 9, No. 5-6, pp. 564-569.
Publisher: JOHN WILEY & SONS LTD, BAFFINS LANE CHICHESTER, W SUSSEX, ENGLAND PO19 1UD.
ISSN: 0952-3499.
DOCUMENT TYPE: Article; Journal

LANGUAGE: English
REFERENCE COUNT: 14
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A peptide mimicking protein A for its ability to recognize the Fc immunoglobulin portion has been identified through screening of a synthetic multimeric peptide library, Screening of the multimeric library, composed of randomized synthetic tripeptide tetramers, has been carried out using a very simple assay, measuring the library ability to interfere with the interaction between protein A and biotinylated immunoglobulins, monitored on solid phase using an enzyme-linked immunosorbent assay format, The tetrameric tripeptide identified after three screening cycles was produced in larger amounts and then immobilized in high yield on preactivated solid support for the preparation of affinity columns, which proved useful for a very convenient one-step purification of antibodies directly from crude sera, Antibody purity after affinity purification was close to 95 per cent, as determined by densitometric scanning of sodium dodecyl sulphate-polyacrylamide gel electrophoresis gels of purified fractions, and up to 2 mg of antibody could be purified from 1 ml of **peptide-derivatized** affinity support. The **ligand** was stable to treatment with a vast array of sanitation agents, such as ethanol and 0.1 M sodium hydroxide, and to repeated use, thus making the **ligand** applicability extremely attractive for the purification of monoclonal antibodies for therapeutic use, Column binding selectivity was similar to that of protein A-affinity columns, since immunoglobulin G from several sources (rabbit, goat, sheep, mouse) was conveniently purified, with no detection of leaked **ligand** fragments in the purified preparations.

L12 ANSWER 4 OF 4 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 2
ACCESSION NUMBER: 95362110 EMBASE
DOCUMENT NUMBER: 1995362110
TITLE: On-line solid-phase synthesis of a peptide bi-derivatized with biotin and 4-azido salicylic acid.
AUTHOR: Lelievre D.; Daguet D.; Brack A.
CORPORATE SOURCE: Centre de Biophysique Moleculaire, Rue Charles Sadron, 45071 Orleans Cedex 2, France
SOURCE: Tetrahedron Letters, (1995) 36/51 (9317-9320).
ISSN: 0040-4039 CODEN: TELEAY
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The peptide (TSP)4 is an efficient substrate for GalNAc transferase. To localize the active site of GalNAc transferase. Biotin-(TSP)4-Lys(ASA)-G was prepared by on-line solid phase synthesis using Fmoc strategy. The new protecting group, 1-(4,4-dimethyl-2,6-dioxycyclohexy-1-ylidene)ethyl (Dde) was used as a temporary protecting group for N(ε)-lysine. The bi-**derivatized peptide** was characterized by mass spectrometry and FTIR spectrometry. This strategy can be generalized to other bi-derivatized peptides synthesized for **ligand-receptor** studies.

=> d his

(FILE 'HOME' ENTERED AT 17:50:58 ON 18 MAY 2004)

FILE 'MEDLINE, BIOSIS, EMBASE, SCISEARCH, CAPLUS, WPIDS' ENTERED AT 17:51:26 ON 18 MAY 2004
L1 270426 S RECEPTOR AND LIGAND
L2 11 S L1 AND (FORMYLATED(A)PEPTIDE)

```
L3            6 DUP REM L2 (5 DUPLICATES REMOVED)
L4         1186 S L1 AND MULTIVALENT
L5           42 S L4 AND G(A)PROTEIN
L6           15 DUP REM L5 (27 DUPLICATES REMOVED)
L7        16240 S L1 AND G(A)PROTEIN
L8          312 S L4 AND ((T(A)CELL) OR (B(A)CELL) OR NEUTROPHIL OR LYMPHOCYTE
L9           20 S L8 AND (SCAFFOLD OR SCAFFOLDING OR ARRAY OR ARRAYS)
L10           9 DUP REM L9 (11 DUPLICATES REMOVED)
L11           9 S L1 AND (DERIVATIZED(A)PEPTIDE)
L12           4 DUP REM L11 (5 DUPLICATES REMOVED)

=> s l1 and formyl
L13       1324 L1 AND FORMYL

=> s l1 and formyl(a)peptide
L14        894 L1 AND FORMYL(A) PEPTIDE

=> s l14 and l4
L15          0 L14 AND L4

=> s l14 and (scaffold or scaffolding or array or arrays)
L16          6 L14 AND (SCAFFOLD OR SCAFFOLDING OR ARRAY OR ARRAYS)

=> dup rem
ENTER L# LIST OR (END):l16
PROCESSING COMPLETED FOR L16
L17          6 DUP REM L16 (0 DUPLICATES REMOVED)

=> d ibib abs l17 1-6

L17  ANSWER 1 OF 6  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2004:93934  CAPLUS
DOCUMENT NUMBER:          140:162333
TITLE:                    Chemotaxis and calcium responses of phagocytes to
                          formyl peptide receptor
                          ligands is differentially regulated by cyclic ADP
                          ribose
AUTHOR(S):                Partida-Sanchez, Santiago; Iribarren, Pablo;
                          Moreno-Garcia, Miguel E.; Gao, Ji-Liang; Murphy,
                          Philip M.; Oppenheimer, Norman; Wang, Ji Ming; Lund,
                          Frances E.
CORPORATE SOURCE:         Trudeau Institute, Saranac Lake, NY, 12983, USA
SOURCE:                   Journal of Immunology (2004), 172(3), 1896-1906
                          CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER:                American Association of Immunologists
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Cyclic ADP ribose (cADPR) is a calcium-mobilizing metabolite that
     regulates intracellular calcium release and extracellular calcium influx.
     Although the role of cADPR in modulating calcium mobilization has been
     extensively examined, its potential role in regulating immunol. responses is
     less well understood.  The authors previously reported that cADPR,
     produced by the ADP-ribosyl cyclase, CD38, controls calcium influx and
     chemotaxis of murine neutrophils responding to fMLF, a peptide agonist for
     two chemoattractant receptor subtypes, formyl
     peptide receptor and formyl peptide
     receptor-like 1.  Here, they examine whether cADPR is required for
     chemotaxis of human monocytes and neutrophils to a diverse array
     of chemoattractants.  They found that a cADPR antagonist and a CD38
     substrate analog inhibited the chemotaxis of human phagocytic cells to a
     number of formyl peptide receptor-like
     1-specific ligands but had no effect on the chemotactic response of these
     cells to ligands selective for formyl peptide
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receptor. In addition, the authors show that the cADPR antagonist blocks the chemotaxis of human monocytes to CXCR4, CCR1, and CCR5 ligands. In all cases, the authors found that cADPR modulates intracellular free calcium levels in cells activated by chemokines that induce extracellular calcium influx in the apparent absence of intracellular calcium release. Thus, cADPR regulates calcium signaling of a discrete subset of chemoattractant receptors expressed by human leukocytes. Since many of the chemoattractant receptors regulated by cADPR bind to ligands that are associated with clin. pathol., cADPR and CD38 represent novel drug targets with potential application in chronic inflammatory and neurodegenerative disease.

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:532691 CAPLUS
DOCUMENT NUMBER: 139:95435
TITLE: Modified receptors on cell membranes for the discovery of therapeutic ligands
INVENTOR(S): Schwartz, Thue W.; Martini, Lene; Heydorn, Arne; Jorgensen, Rasmus
PATENT ASSIGNEE(S): 7TM Pharma A/S, Den.
SOURCE: PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003055914	A2	20030710	WO 2002-DK900	20021220
WO 2003055914	A3	20031023		

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

DK 2001-1944	A	20011221
DK 2002-113	A	20020122
DK 2002-1043	A	20020703
US 2002-394122P	P	20020703

AB A drug discovery method is provided for selecting a compound selected from the group consisting of a small organic substance, a biopharmaceutical, or an antibody or part thereof. The method comprises the steps of (i) expressing one or more receptors on a cell membrane, such as, e.g., an exterior cell surface of a cell, (ii) contacting one or more expressed receptors with a test compound or a selection of test compds. (libraries), and (iii) selecting one or more compds. based on its ability to bind one or more receptors. The step of expressing the one or more receptors comprises capturing one or more receptors on the exterior cell surface in a conformation that predominantly enables binding or interaction with a **ligand**, and the conformation that predominantly enables binding or interaction with a **ligand** is provided by modification of one or more receptors by a method comprising at least one of the following: (a) fusion with any protein which keeps the **receptor** in the desired conformation such as, e.g. an arrestin, a modified arrestin, a G-protein

or a modified G-protein, (b) site-directed mutagenesis, and (c) deletion. The receptors may be captured on the exterior cell surface by at least one of the following: (d) interaction of the **receptor** with a **scaffolding** protein, optionally, with a **scaffolding** protein network and (e) means for blocking **receptor** internalization, e.g. by co-expression of a mutated dynamin or a modified arrestin or by use of chems. such as, e.g., sucrose and/or Tris. Thus, by coexpressing of either the wild-type **receptor** or by modifying the **receptor** by engineering for example a recognition motif for a strong binder into its structure (for example, a PDZ recognition motif at its C-terminal end), and coexpression of this with a **scaffolding** protein such as PSD-95 or a modified **scaffolding** protein which interacts with the cytoskeleton at the cell surface or is made to be closely associated with the membrane through a lipid anchor, a high level of surface expression can be ensured, which will benefit its use in the drug discovery process. As a result of the strong tendency of the **scaffolding** proteins to interact with each other, just the cotransfection with one or more appropriate **scaffolding** proteins or modified **scaffolding** protein may also lead to the formation of patches with high local concns of the **receptor** or modified **receptor**, which will be highly beneficial in the drug discovery process where they are used initially to select binding mols. The method is exemplified by expression of the NK1 **receptor** in an agonist high-affinity binding form at the surface of transfected cells through fusion with arrestin or the N-terminal fragment of arrestin.

L17 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:301250 CAPLUS
DOCUMENT NUMBER: 138:298915
TITLE: Genes and proteins for prevention, prediction, prognosis and therapy of cardiovascular disease
INVENTOR(S): Munnes, Marc; Gehrmann, Mathias; Wick, Maresa; Schmitz, Gerd
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany; Bayer Healthcare AG
SOURCE: PCT Int. Appl., 446 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003031650	A2	20030417	WO 2002-EP11034	20021002
WO 2003031650	A3	20040212		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2001-24145 A 20011008

AB Genes that are differentially expressed in blood vessels of cardiovascular disease patients vs. blood vessels of normal people are disclosed. Specifically, 74 genes genes are identified that are differentially expressed in cardiovascular disease states, relative to their expression in normal, and/or in response to manipulations relevant to cardiovascular

disease (e.g., incubation of isolated macrophages in the presence of enzymically modified LDL). In particular, genes that are up- or down-regulated in macrophages of patients with inherited predisposition for arteriosclerosis are disclosed by the differential expression approach with DNA **array** technol. and TaqMan anal. The genes provide novel methods, uses and compns. for the prediction, prevention, diagnosis, prognosis, and treatment of cardiovascular disease.

L17 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:314864 CAPLUS
DOCUMENT NUMBER: 132:344076
TITLE: Method for detecting endocrine disruptor-responsive genes and for screening endocrine disruptors
INVENTOR(S): Kondo, Akihiro; Sagawa, Hiroaki; Mineno, Junichi; Kimizuka, Fusao; Kato, Ikunoshin
PATENT ASSIGNEE(S): Takara Shuzo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000026404	A1	20000511	WO 1999-JP5964	19991028
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9964878	A1	20000522	AU 1999-64878	19991028
EP 1126035	A1	20010822	EP 1999-952794	19991028
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: JP 1998-310285 A 19981030
WO 1999-JP5964 W 19991028

AB A method and compns. for detecting genes affected by endocrine-disrupting chems. and for identifying endocrine-disrupting chems. are claimed. The method comprises preparing a nucleic acid sample containing mRNAs or cDNAs originating in cells, tissues, or organisms which have been brought into contact with a sample containing the endocrine disruptor. The nucleic acid sample is hybridized with DNA **arrays** wherein genes which might be affected by the endocrine disruptor or DNA fragments originating in these genes have been fixed. The results obtained are then compared with the results obtained with the control sample to select the gene affected by the endocrine disruptor. Endocrine disruptors are selected from dioxins, organic chloro compds., phenols, futalic acid esters, aromatic hydrocarbons, agrochems., organic tin compds., and estrogens, among others. The effect of 3 chems., 17-β estradiol (E2), diethylstilbestrol (DES), and bisphenol A (BisA) on 33 candidate genes belonging to the categories of nuclear **receptor**/nuclear **receptor** transcriptional coupling, kinase-type signal transducer, gonad differentiation factor, oncogene, and **receptor**-type kinase, were examined by the method of this invention. Expression of most of the genes was either increased or decreased by exposure to these chems.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:873648 CAPLUS
DOCUMENT NUMBER: 135:105834
TITLE: Analysis of mucosal gene expression in inflammatory bowel disease by parallel oligonucleotide **arrays**
AUTHOR(S): Dieckgraefe, B. K.; Stenson, W. F.; Korzenik, J. R.; Swanson, P. E.; Harrington, C. A.
CORPORATE SOURCE: Division of Gastroenterology and Department of Surgical Pathology, Washington University School of Medicine, St. Louis, MO, 63110, USA
SOURCE: Physiological Genomics [online computer file] (2000), 4, 1-11
CODEN: PHGEFP; ISSN: 1094-8341
URL: http://physiolgenomics.physiology.org/cgi/reprint/4/1/1.pdf
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB DNA **arrays** capable of simultaneously measuring expression of thousands of genes in clin. specimens from affected and normal individuals have the potential to provide information about disease pathogenesis not previously possible. Few studies have applied mRNA profiling to diseases involving complex tissues like the intestinal mucosa, reflecting the unique challenges inherent to this type of anal. We report the anal. of mucosal gene expression in ulcerative colitis (UC) patients and inflamed and noninflamed control specimens. Genes can be used as markers for cell recruitment, activation, and mucosal synthesis of immunoregulatory mols. Self-organizing maps were applied to cluster and analyze gene expression patterns and were paired with histopathol. scores to identify genes associated with increased disease activity. Clustering was achieved on the basis of differences in expression levels across individual specimens. Several inflammatory mediators were identified as likely determinants of characteristic histol. features of active UC. These results provide proof of principle for application of functional genomics to larger inflammatory bowel disease populations for gene discovery, to facilitate identification of disease subgroups on the basis of gene expression signatures, and for prediction of disease behavior or optimal therapeutic intervention.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 6 OF 6 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 96:910803 SCISEARCH
THE GENUINE ARTICLE: VW615
TITLE: Molecular cloning of a novel **receptor** (CMKLR1) with homology to the chemotactic factor receptors
AUTHOR: Gantz I (Reprint); Konda Y; Yang Y K; Miller D E; Dierick H A; Yamada T
CORPORATE SOURCE: UNIV MICHIGAN, MED CTR, DEPT SURG, 6504 MSRB I, 1150 W MED CTR DR, ANN ARBOR, MI 48109 (Reprint); UNIV MICHIGAN, MED CTR, DEPT INTERNAL MED, ANN ARBOR, MI 48109; UNIV MICHIGAN, MED CTR, DEPT PEDIAT, ANN ARBOR, MI 48109; UNIV MICHIGAN, MED CTR, DEPT PHYSIOL, ANN ARBOR, MI 48109
COUNTRY OF AUTHOR: USA
SOURCE: CYTOGENETICS AND CELL GENETICS, (SEP 1996) Vol. 74, No. 4, pp. 286-290.
Publisher: KARGER, ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND.
ISSN: 0301-0171.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 30

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We report the cloning of a novel human gene, CMKLR1, which encodes a protein that has notable sequence and structural homology to the seven transmembrane G-protein linked chemokine receptors. This gene has 55% nucleotide sequence homology to the IL-8 type I **receptor** and 53% to the N-**formyl peptide** related **receptor** 1 genes. The mRNA of this **receptor** is expressed in a broad **array** of tissues associated with hematopoietic and immune function including, spleen, thymus, appendix, lymph node, bone marrow, and fetal liver. Using fluorescence in situ hybridization the gene encoding CMLKR1 (chemokine-like **receptor** 1) was localized to human chromosome 12q24.1.

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-9.01	-9.01

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                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.42       0.42

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FILE 'BIOSIS' ENTERED AT 16:53:00 ON 18 MAY 2004
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=> e Kiessling
E1            1     KIESSLGUHR/BI
E2            1     KIESSLICH/BI
E3           54 --> KIESSLING/BI
E4            1     KIESSLSAUREAUSSCHEIDUNG/BI
E5            2     KIESSWETTER/BI
E6            3     KIEST/BI
E7           12     KIESTER/BI
E8            1     KIESTERBACH/BI
E9            3     KIESTERI/BI
E10           1     KIESTLER/BI
E11           2     KIESTRA/BI
E12           1     KIESTRUS/BI

=> s e3
L1           54 KIESSLING/BI

=> dup rem
ENTER L# LIST OR (END):l1
PROCESSING COMPLETED FOR L1
L2            44 DUP REM L1 (10 DUPLICATES REMOVED)

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L2   ANSWER 1 OF 44  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Crystalline muscle phosphorylase: I. Preparation, properties, and
     molecular weight
AB   In 1936 glucose-1-phosphate was isolated from minced and washed frog
     muscle which had been incubated in phosphate buffer with traces of
     adenylic acid (1).  It was shown that the ester was formed from glycogen
     by the reaction, glycogen + inorg. phosphate → glucose-1-phosphate.
     The enzyme which catalyzed this reaction was called phosphorylase; its
     presence in mammalian tissues (muscle, heart, brain, liver) and in yeast
     was demonstrated (2); phosphorylase was shown to play an important role in
     the formation of blood sugar in the liver (3).  In 1939 the reversibility
     of the reaction was shown for yeast phosphorylase by Kiessling
     (4) and for the mammalian phosphorylases by Cori, Schmidt, and Cori (5).
     In 1940 Hanes (6) described the presence of phosphorylase in peas and
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potatoes. The polysaccharide synthesized by muscle phosphorylase resembles the amylose fraction of natural starch (7), while the enzymes from the other mammalian tissues (8) and from yeast (9) form a polysaccharide which resembles glycogen. Potato phosphorylase synthesizes a polysaccharide which resembles amylose (10). Cori and Cori (11) showed that phosphorylases of mammalian origin require the presence of polysaccharide for polysaccharide synthesis, and this was confirmed by Hanes (12) for plant phosphorylase. His claim that maltose could be substituted for polysaccharide was not confirmed by Green and Stumpf (13) nor by work done in this laboratory, when care was taken to free the maltose of polysaccharide impurities. Cori, Colowick, and Cori (14) found that phosphorylases derived from vertebrate tissues required the addition of adenylic acid as coenzyme, while yeast (9) and potato (13) phosphorylases were shown to be active in the absence of added adenylic acid. Reducing agents (glutathione, cysteine, KCN) were shown to increase the activity of muscle phosphorylase (15), while they are without effect on potato phosphorylase (13). The crystallization of muscle phosphorylase was announced in

a preliminary note (16). The present paper deals with the method of preparation of the crystalline enzyme and some of its properties.

L2 ANSWER 2 OF 44 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
TI On a class of elliptic problems in R-2: symmetry and uniqueness results
AB In the plane R-2, we classify all solutions for an elliptic problem of Liouville type involving a (radial) weight function. As a consequence, we clarify the origin of the non-radially symmetric solutions for the given problem, as established by Chanillo and **Kiessling.**

For a more general class of Liouville-type problems, we show that, rather than radial symmetry, the solutions always inherit the invariance, of the problem under inversion with respect to suitable circles. This symmetry result is derived with the help of a 'shrinking-sphere' method.

L2 ANSWER 3 OF 44 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI Change of ultraviolet absorbance of sunscreens by exposure to solar-simulated radiation.
CO Laboratoires garnier (France); **E kiessling and cie gmbh (Germany)** ; Bayer (Germany); Roche Posay (France); Beiersdorf (Germany); Tiroler nussol sonnenkosmetik (Germany); P and g (United Kingdom); Sara Lee (Germany); Vichy Farmacosmetici (France); Johnson and Johnson (Germany); Bubchen werk ewald hermes pharmazeutische fabrik gmbh (Germany)

L2 ANSWER 4 OF 44 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
TI Zeros of wave functions in Ginzburg-Landau model for small epsilon
AB In this paper we study zeros of condensate wave functions in Ginzburg-Landau model. The main question we are concerned with is when a condensate wave function appears to have only isolated zeros of degree one. Our main result shows that under some conditions on the energy and the tension field a condensate wave function will appear to possess only the expected number of isolated zeros of degree one. We will also discuss how the heat Bow can deform a condensate wave function and make it appear to possess the expected number of isolated zeros of degree one. In the end we will mention a slight improvement of a uniqueness result of Chanillo and **Kiessling.**

L2 ANSWER 5 OF 44 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
TI Johann **Kiessling,** the Krakatoa event and the development of atmospheric optics after 1883
TI Johann **Kiessling,** the Krakatoa event and the development of atmospheric optics after 1883

L2 ANSWER 6 OF 44 MEDLINE on STN DUPLICATE 1
TI Escape mechanisms in tumor immunity: a year 2000 update.

AB The current consensus of opinion has it that most or possibly all tumors, spontaneous as well as induced, are immunogenic, expressing antigens in a form recognizable by the host immune system. Accordingly, in order to progress, tumors have to evolve strategies for evading immune responses. The purpose of this review is to consider the current status of knowledge concerning these different tumor escape strategies. It represents an update of an article originally published in this journal in 1997 (Pawelec, Zeuthen, and **Kiessling**, 1997). Therefore, it focuses mostly on publications that have appeared since then, illustrating the impressive accumulation of new data since that time and the importance currently attributed to studies of tumor escape from the immune response.

L2 ANSWER 7 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI The 2000 Horace S. Isbell award
AB Laura L. **Kiessling** is the recipient of the Horace S. Isbell Award 2000. The award is in recognition of the accomplishments of carbohydrate scientists who have not yet reached their 41st birthday. **Kiessling**'s research focuses on elucidating and exploiting the mechanisms of cell surface recognition processes, especially those that involve protein-saccharide recognition and oligosaccharide function.
ST award **Kiessling**
IT Awards
(Horace S. Isbell Award; Laura L. **Kiessling** received the Horace S. Isbell Award 2000)

L2 ANSWER 8 OF 44 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
TI **Kiessling**: Seeing connections
TI **Kiessling**: Seeing connections

L2 ANSWER 9 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
TI Arthur C. Cope Scholars
AB Laura L. **Kiessling** received the Arthur C. Cope Scholars award for her achievements in organic chemical and biochem.
ST **Kiessling** Arthur Cope Scholar award biochem

L2 ANSWER 10 OF 44 MEDLINE on STN DUPLICATE 2
TI Structural changes in subdomain 2 of G-actin observed by fluorescence spectroscopy.
AB The influence of DNase I binding to Ca-ATP-G-actin and of Ca2+/Mg2+ and ATP/ADP exchange on the conformation of G-actin were investigated by measuring the fluorescence of dansyl cadaverine (DC) conjugated to Gln41 in subdomain 2 of the protein. Fluorescence resonance energy transfer (FRET) between this probe and N-[4-(dimethylamino)-3,5-dinitrophenyl]maleimide (DDPM) attached to Cys374 in subdomain 1 was also measured. Contrary to an earlier report [dos Remedios, **Kiessling** and Hambly (1994) in Synchrotron Radiation in the Biosciences (Chance, B., Deisenhofer, J., Ebashi, S., Goodhead, D. T., Helliwell, J. R., Huxley, H. E., Iizuka, T., Kirz, J., Mitsui, T., Rubenstein, E. et al., eds.), pp. 418-425, Oxford University Press, Oxford], the distance between these probes did not change significantly when DNase I was bound to actin. A